EXAMINER NOTES

STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 133771

TO: Rebecca Cook **Location: REM-3C70** **Art Unit: 1614** **Wednesday, September 29, 2004** **Case Serial Number: 10/623431**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **Remsen 1A69** **Phone: 571-272-2518** BOB **barbara.obryen@uspto.gov**

Search Notes

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Dave O'Bryen

133771

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

RECEIVED
SEP 28 2004
(STIC)

Requestor's Name: Rebecca Cook

Serial Number: 10/823431

Date: 9/28/04

Phone: Rem 3C70

Art Unit: 1614

Search Topic: Gary Kranzler S. Rao

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please search the compound of claim 27

& the generic ~~[illegible]~~ SNRI (claim 26)

to treat pain, FMS, CFS.

Thanks

Rebecca

STAFF USE ONLY

Date completed: 9-29-04

Searcher: Bob

Terminal time: 35

Elapsed time: prep 25

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

1 Structure

_____ Bibliographic

Vendors

_____ IG

440 STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

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=> fil reg; d stat que l9; fil capl; d que nos l21; fil uspatf; d que nos l26; fil
embase; d que nos l39; fil medl; d que nos l31
FILE 'REGISTRY' ENTERED AT 14:39:51 ON 29 SEP 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 SEP 2004  HIGHEST RN 753424-73-6
DICTIONARY FILE UPDATES:  28 SEP 2004  HIGHEST RN 753424-73-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L7                STR
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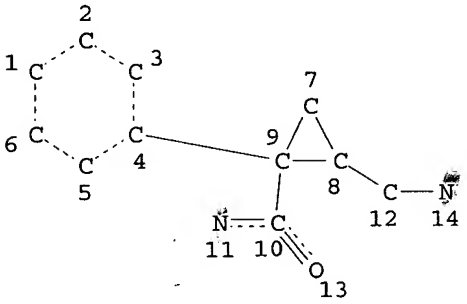

= ring or chain node

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NODE ATTRIBUTES:
NSPEC   IS RC     AT  11
NSPEC   IS RC     AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L9          355 SEA FILE=REGISTRY SSS FUL L7

100.0% PROCESSED    669 ITERATIONS                    355 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 14:39:51 ON 29 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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```

FILE COVERS 1907 - 29 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L7              STR
L9          355 SEA FILE=REGISTRY SSS FUL L7
L17       13224 SEA FILE=CAPLUS ABB=ON  PAIN/CT
L18         693 SEA FILE=CAPLUS ABB=ON  CHRONIC/OBI(L)FATIGUE/OBI OR MYALGIC
                ENCEPHALOMYELITIS/OBI
L19         513 SEA FILE=CAPLUS ABB=ON  FIBROMYALGI?/OBI OR FIBROSITIS/OBI OR
                MUSCULAR/OBI(L)RHEUMAT?/OBI OR MYOFASCIAL PAIN/OBI OR FIBROMYOS
                ITI?/OBI
L20         230 SEA FILE=CAPLUS ABB=ON  L9
L21          16 SEA FILE=CAPLUS ABB=ON  L20 AND (L17 OR L18 OR L19)
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FILE 'USPATFULL' ENTERED AT 14:39:51 ON 29 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 28 Sep 2004 (20040928/PD)
FILE LAST UPDATED: 28 Sep 2004 (20040928/ED)
HIGHEST GRANTED PATENT NUMBER: US6799328
HIGHEST APPLICATION PUBLICATION NUMBER: US2004187181
CA INDEXING IS CURRENT THROUGH 28 Sep 2004 (20040928/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 28 Sep 2004 (20040928/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2004

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<

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>>>                                                                  <<<
>>>  Use USPATALL when searching terms such as patent assignees,     <<<
>>>  classifications, or claims, that may potentially change from   <<<
>>>  the earliest to the latest publication.                         <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L7              STR
L9          355 SEA FILE=REGISTRY SSS FUL L7
L22          59 SEA FILE=USPATFULL ABB=ON  L9
L23         275 SEA FILE=USPATFULL ABB=ON  (FIBROMYALGI? OR FIBROSITIS OR
                MUSCULAR(L)RHEUMAT? OR MYOFASCIAL PAIN OR FIBROMYOSITI?)/IT
L24         311 SEA FILE=USPATFULL ABB=ON  (CHRONIC(L)FATIGUE OR MYALGIC
                ENCEPHALOMYELITIS)/IT
L25        1537 SEA FILE=USPATFULL ABB=ON  PAIN/CT
L26          11 SEA FILE=USPATFULL ABB=ON  L22 AND (L23 OR L24 OR L25)



FILE 'EMBASE' ENTERED AT 14:39:51 ON 29 SEP 2004
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 FILE COVERS 1974 TO 24 Sep 2004 (20040924/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L7              STR
L9          355 SEA FILE=REGISTRY SSS FUL L7
L32         370 SEA FILE=EMBASE ABB=ON  L9
L33      243807 SEA FILE=EMBASE ABB=ON  PAIN+NT/CT
L34        3239 SEA FILE=EMBASE ABB=ON  FIBROMYALGIA/CT OR FIBROMYALGIA
                SYNDROME/CT
L35        2867 SEA FILE=EMBASE ABB=ON  CHRONIC FATIGUE SYNDROME/CT
L38       42518 SEA FILE=EMBASE ABB=ON  (L33 OR L34 OR L35)(L)(DT OR PC)/CT
L39          19 SEA FILE=EMBASE ABB=ON  L32 AND L38
                                        DT = drug therapy
                                        PC = prevention

FILE 'MEDLINE' ENTERED AT 14:39:51 ON 29 SEP 2004

 FILE LAST UPDATED: 28 SEP 2004 (20040928/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L7              STR
L9          355 SEA FILE=REGISTRY SSS FUL L7
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L27          109 SEA FILE=MEDLINE ABB=ON  L9
L28       170781 SEA FILE=MEDLINE ABB=ON  PAIN+NT/CT
L29         2830 SEA FILE=MEDLINE ABB=ON  FIBROMYALGIA/CT
L30         2518 SEA FILE=MEDLINE ABB=ON  FATIGUE SYNDROME, CHRONIC/CT
L31            6 SEA FILE=MEDLINE ABB=ON  L27 AND (L28 OR L29 OR L30)


=> dup rem l21,l26,l31,l39
FILE 'CAPLUS' ENTERED AT 14:39:58 ON 29 SEP 2004
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FILE 'USPATFULL' ENTERED AT 14:39:58 ON 29 SEP 2004
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FILE 'MEDLINE' ENTERED AT 14:39:58 ON 29 SEP 2004

FILE 'EMBASE' ENTERED AT 14:39:58 ON 29 SEP 2004
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PROCESSING COMPLETED FOR L21
PROCESSING COMPLETED FOR L26
PROCESSING COMPLETED FOR L31
PROCESSING COMPLETED FOR L39
L42           44 DUP REM L21 L26 L31 L39 (8 DUPLICATES REMOVED)
                 ANSWERS '1-16' FROM FILE CAPLUS
                 ANSWERS '17-23' FROM FILE USPATFULL
                 ANSWERS '24-28' FROM FILE MEDLINE
                 ANSWERS '29-44' FROM FILE EMBASE

=> d ibib ed abs hitstr 1-23; d iall 24-44

L42  ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:392318  CAPLUS
DOCUMENT NUMBER:          140:400077
TITLE:                    Pharmaceutical combinations including either a 5-HT4
                          receptor agonist or antagonist or a 5-HT3 receptor
                          antagonist and a co-agent and their use in treating
                          gastrointestinal and abdominal visceral disorders
INVENTOR(S):              Billstein, Stephan Anthony; Dumovic, Peter; Franco,
                          Nicola; Iwicki, Mark Thomas; Pfannkuche, Hans-Jurgen;
                          Wilusz, Edward Joseph
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S.
                          Ser. No. 722,784, abandoned.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 2004092511         A1    20040513    US 2003-702688           20031106
PRIORITY APPLN. INFO.:                       US 1999-266333P      P   19991210
                                             US 2000-722784       B1  20001127
ED   Entered STN:  14 May 2004
AB   The invention discloses a combination of a first agent including either a
     5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a
     co-agent and pharmaceutical compns. and formulations contg. the
     combination.  The invention also discloses a method for treating a
     gastrointestinal and abdominal visceral disorder by administering the
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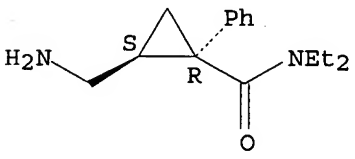
pharmaceutical compns. to a patient. The pharmaceutical compns. may also be employed as laxatives, to prep. a patient for colonoscopy and to regulate and stabilize enterochromaffin cell secretory, pain and motility mechanisms, afferent fiber activity and GI and lower abdominal smooth muscle cells. The dosage is preferably oral and administration is preferably once or twice a day. The preferred first agent is tegaserod.

IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:353140 CAPLUS
DOCUMENT NUMBER: 140:380634
TITLE: Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or prevention of neuropathic pain
INVENTOR(S): Cheung, Raymond Y.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082543	A1	20040429	US 2002-282660	20021029
WO 2004039371	A2	20040513	WO 2003-US33089	20031017
WO 2004039371	A3	20040617		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-282660 A 20021029
OTHER SOURCE(S): MARPAT 140:380634
ED Entered STN: 30 Apr 2004

AB The present invention provides compns. and methods to treat or prevent

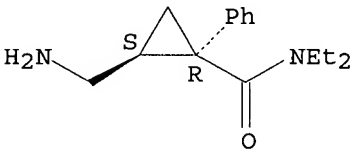
neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.

IT **92623-85-3**, Milnacipran
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 3 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:142815 CAPLUS
DOCUMENT NUMBER: 140:157480
TITLE: Monoamine reuptake inhibitors for the treatment and prevention of depression secondary to pain
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 28,547.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004034101	A1	20040219	US 2003-628141	20030724
US 2003139476	A1	20030724	US 2001-14149	20011105
US 6635675	B2	20031021		
US 2003130353	A1	20030710	US 2001-28547	20011219
US 6602911	B2	20030805		

PRIORITY APPLN. INFO.:

US 2001-14149	A2	20011105
US 2001-28547	A2	20011219
US 2002-398676P	P	20020724
US 2003-443035P	P	20030128

ED Entered STN: 22 Feb 2004

AB Methods for the prevention or treatment of a typical depression secondary to pain (DSP) have been developed. The method generally involves administering an effective amt. of a monoamine reuptake inhibitor to treat or prevent symptoms of DSP. In a preferred embodiment, a therapeutically effective amt. of a dual serotonin/norepinephrine reuptake inhibitor (SNRI) compd. of a specific type, or a pharmaceutically acceptable salt thereof, is administered. The most preferred SNRI compds. are non-tricyclic SNRIs, wherein serotonin reuptake inhibition is greater than norepinephrine reuptake inhibition; and NSRIs, wherein norepinephrine reuptake inhibition is greater than serotonin reuptake inhibition. The most preferred compd. is milnacipran, or a bioequivalent or pharmaceutically acceptable salt thereof. Other preferred compds. are duloxetine and venlafaxine or a bioequivalent or pharmaceutically acceptable salt thereof. In yet another embodiment, a therapeutically

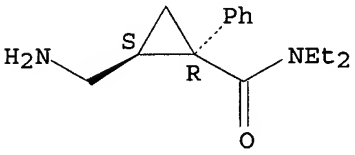
effective amt. of a non-tricyclic triple reuptake inhibitor (TRI) compd. of a specific type, or a pharmaceutically acceptable salt thereof, is administered. The TRI compds. are characterized by their ability to block the reuptake (and hence increase central concns. of) the three primary brain monoamines: serotonin, noradrenaline, and dopamine.

IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoamine reuptake inhibitors for treatment and prevention of depression secondary to pain)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2004:315145 CAPLUS

DOCUMENT NUMBER: 141:218781

TITLE: An open-label clinical trial of milnacipran in **fibromyalgia** syndrome with co-morbid depressive symptoms

AUTHOR(S): Nagaoka, Shouhei; Ohno, Mikako; Sekiguchi, Akiko

CORPORATE SOURCE: Department of Rheumatology, Yokohama Minami Kyosai Hospital, Kanagawa, Japan

SOURCE: International Journal of Psychiatry in Clinical Practice (2004), 8(1), 47-51
CODEN: IJPCFZ; ISSN: 1365-1501

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 19 Apr 2004

AB OBJECTIVE: To evaluate the efficacy of the serotonin and noradrenaline reuptake inhibiting antidepressant, milnacipran, in patients with fibromyalgia syndrome and comorbid depression. METHODS: Twenty patients with fibromyalgia syndrome and comorbid depressive symptoms were treated with the serotonin and noradrenaline reuptake inhibitor, milnacipran, in an open label study. The initial dose of milnacipran was 30 mg/day which could be increased as needed up to 100 mg/day. Patients were evaluated at baseline and after 4, 8 and 12 wk of treatment. Pain level and global symptomatol. were detd. using visual analog scales. Pain was also accessed by use of the face scale, while the severity of depression was detd. using the Zung self-rating depression scale. RESULTS: Two patients withdrew because of persistent nausea. Pain and general symptomatol. were significantly improved at the end of the study, with five patients having a redn. in pain of greater than 50%. Posthoc anal. showed that the 11 patients who were no longer depressed at the end of the study had the greatest improvement in pain and overall FMS symptomatol. CONCLUSION: The data suggest that milnacipran may be effective in the treatment of FMS, esp. when assocd. with depression.

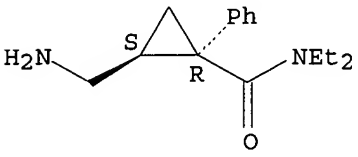
IT **101152-94-7**, Milnacipran hydrochloride
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Ixel, Toledomin, Dalcipran; milnacipran in **fibromyalgia** syndrome with co-morbid depressive symptoms)

RN 101152-94-7 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, monohydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2003:532350 CAPLUS

DOCUMENT NUMBER: 139:63355

TITLE: Methods using a dual serotonin-norepinephrine reuptake inhibitor for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome, and pain

INVENTOR(S): Kranzler, Jay D.; Rao, Srinivas G.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 14,149.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130353	A1	20030710	US 2001-28547	20011219
US 6602911	B2	20030805		
US 2003139476	A1	20030724	US 2001-14149	20011105
US 6635675	B2	20031021		
WO 2003053426	A1	20030703	WO 2002-US40976	20021219
W: CA, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
US 2004019116	A1	20040129	US 2003-623431	20030718
US 2004034101	A1	20040219	US 2003-628141	20030724

PRIORITY APPLN. INFO.:

US 2001-14149	A2	20011105
US 2001-28547	A1	20011219
US 2002-398676P	P	20020724
US 2003-443035P	P	20030128

ED Entered STN: 11 Jul 2003

AB The invention provides a method of treating fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), and pain in an animal subject. The method generally involves administering a therapeutically effective amt. of a dual serotonin-norepinephrine reuptake inhibitor compd. or a pharmaceutically acceptable salt thereof, wherein the dual

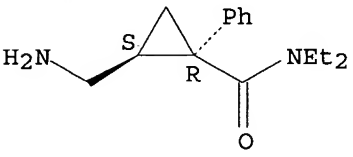
serotonin-norepinephrine reuptake inhibitor compd. is characterized by a non-tricyclic structure and an equal or greater inhibition of norepinephrine reuptake than serotonin reuptake. In particular, the use of milnacipran to treat FMS, CFS, and pain is disclosed.

IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual serotonin-norepinephrine reuptake inhibitor for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome, and pain)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 6 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2003:245946 CAPLUS
DOCUMENT NUMBER: 139:270063
TITLE: New hope in the treatment of painful symptoms in depression
AUTHOR(S): Briley, Mike
CORPORATE SOURCE: NeuroBiz Consulting and Communications, Castres, 81100, Fr.
SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(1), 42-45
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

ED Entered STN: 31 Mar 2003

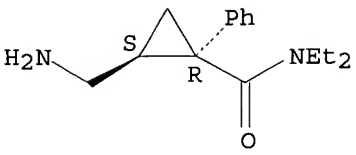
AB A review. Depression is increasingly seen as a triad of psychol., somatic and phys. symptoms that all need to be treated to achieve maximal remission. In primary care, phys. symptoms such as pain, are the principal presenting symptoms, and a common psychopharmacol. between pain and depression suggests that compds. that inhibit the reuptake of both serotonin and norepinephrine are likely to produce the greatest relief from depression and chronic pain. Recent, principally open, trials with members of the new selective serotonin and norepinephrine reuptake inhibitor class of antidepressants such as venlafaxine, milnacipran and duloxetine (Eli Lilly & Co/Shionogi & Co Ltd), suggest that these compds. may be effective in relieving pain both assocd. with, and independent of depression.

IT **92623-85-3**, Milnacipran
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new hope in treatment of painful symptoms in depression)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:392439 CAPLUS
DOCUMENT NUMBER: 140:400095
TITLE: Stereoisomers of p-hydroxy-milnacipran, and therapeutic use
INVENTOR(S): Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.
PATENT ASSIGNEE(S): Collegium Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004039320	A2	20040513	WO 2003-US33681		20031022
WO 2004039320	A3	20040624			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004142904	A1	20040722	US 2003-691465		20031022
PRIORITY APPLN. INFO.:			US 2002-421640P	P	20021025
			US 2002-423062P	P	20021101
			US 2003-445142P	P	20030205

OTHER SOURCE(S): MARPAT 140:400095
ED Entered STN: 14 May 2004
AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prep. a formulation for administration to a patient. Finally,the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising

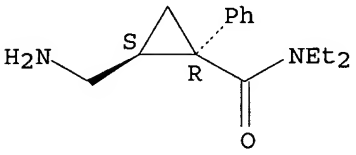
administering to a mammal in need thereof a therapeutically effective amt. of a compd. of the invention. Compd. prepn. is included.

IT **92623-85-3**, Milnacipran
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

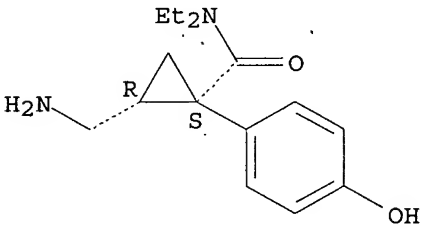


IT **688320-02-7P**, CS 1713 **688320-03-8P**, CS 1714
688320-04-9P, CS 1814
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)

RN 688320-02-7 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, monohydrochloride, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

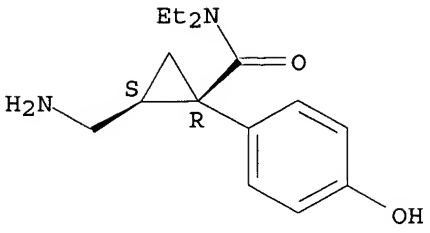


● HCl

RN 688320-03-8 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, monohydrochloride, (1R,2S)- (9CI) (CA INDEX NAME)

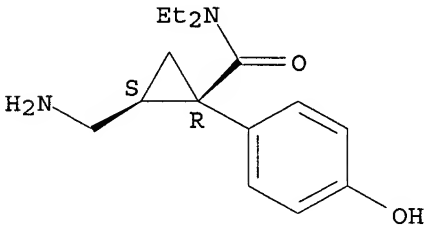
Absolute stereochemistry.



● HCl

RN 688320-04-9 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, monohydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

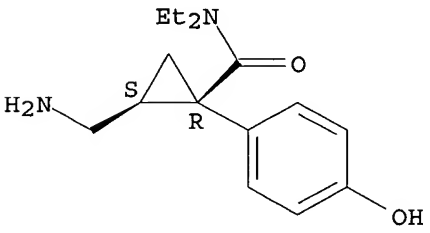
Relative stereochemistry.
Currently available stereo shown.



● HCl

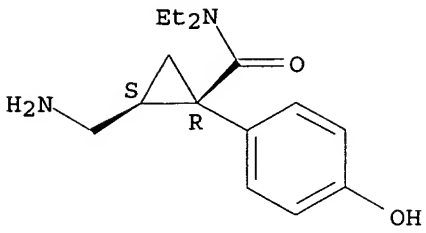
IT **686766-17-6 686766-17-6D**, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)
RN 686766-17-6 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



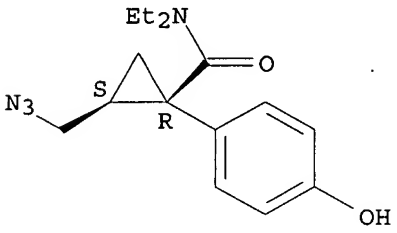
RN 686766-17-6 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



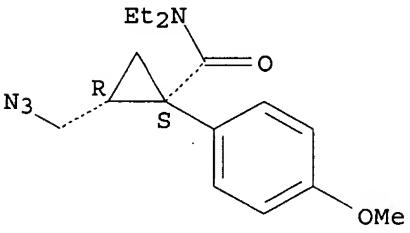
IT **688320-09-4**, CS 1658
RL: RCT (Reactant); RACT (Reactant or reagent)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)
RN 688320-09-4 CAPLUS
CN Cyclopropanecarboxamide, 2-(azidomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



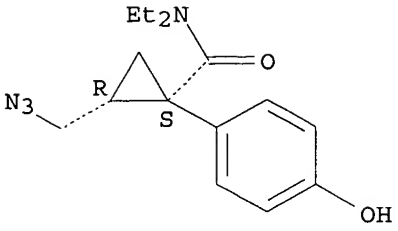
IT **688320-07-2P**, CS 1628 **688320-08-3P**, CS 1649
688738-11-6P, CS 1665 **688738-12-7P**, CS 1710
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)
RN 688320-07-2 CAPLUS
CN Cyclopropanecarboxamide, 2-(azidomethyl)-N,N-diethyl-1-(4-methoxyphenyl)-, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



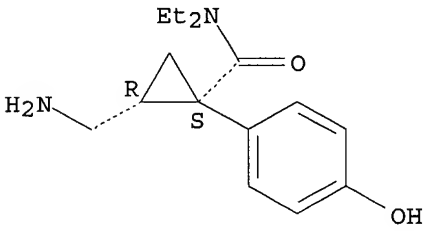
RN 688320-08-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(azidomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



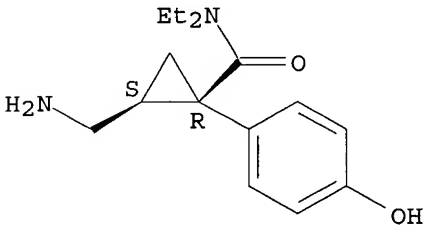
RN 688738-11-6 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1S,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 688738-12-7 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-(4-hydroxyphenyl)-, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L42 ANSWER 8 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:310959 CAPLUS
DOCUMENT NUMBER: 140:297543
TITLE: Dosage escalation and divided daily dose of antidepressants to treat neurological disorders
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.; Gendreau, Michael R.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004030633	A2	20040415	WO 2003-US31622	20031003

WO 2004030633 A3 20040715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004106681 A1 20040603 US 2003-678767 20031003
PRIORITY APPLN. INFO.: US 2002-415739P P 20021003
US 2002-431550P P 20021206
US 2003-443081P P 20030128
US 2003-443203P P 20030128

ED Entered STN: 16 Apr 2004

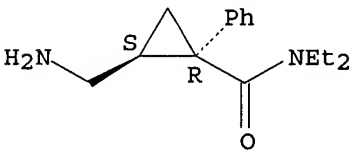
AB The invention provides a method to treat neurol. disorders. The method includes e.g. administering higher daily dosages of antidepressant. The higher daily dosages result in an improved efficacy of the drug, the maintenance of a pos. patient toleration, the maintenance of a pos. patient safety profile (e.g., dose limiting toxicity), a suitable peak plasma concn. (Cmax) of drug, and/or a once-a-day (QD) as opposed to twice-a-day (BID) administration. Increased daily dosages of antidepressant that would normally evoke adverse effects can be administered without the neg. patient tolerability (i.e., adverse reactions) by escalating dosages over time. Such escalation dosages provide more efficacious amts. of antidepressant than would otherwise be permitted. Similarly, higher levels of circulating drug are possible in patients by administering the compd. in divided doses over the course of a day rather than once a day.

IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosage escalation and divided daily dose of antidepressants to treat neurol. disorders)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:80490 CAPLUS
DOCUMENT NUMBER: 140:122820
TITLE: Treatment of depression secondary to pain using milnacipran and other monoamine reuptake inhibitors
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009069	A1	20040129	WO 2003-US23088	20030724

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-398676P P 20020724
US 2003-443035P P 20030128

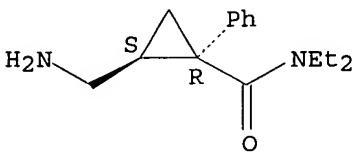
ED Entered STN: 01 Feb 2004

AB The invention discloses the methods for the prevention or treatment of atypical depression secondary to pain (DSP). The method generally involves administering an effective amt. of a monoamine re uptake inhibitor to treat or prevent symptoms of DSP. In a preferred embodiment, a therapeutically effective amt. of a dual serotonin norepinephrine reuptake inhibitor (SRNI) compd. of a specific type, or a pharmaceutically acceptable salt thereof is administered. The most preferred SNRI compds. are non-tricyclic SNRIs, wherein serotonin reuptake inhibition is greater than norepinephrine reuptake inhibition; and NSRIs, wherein norepinephrine reuptake inhibition is greater than serotonin reuptake inhibition. The most preferred compd. is milnacipran or a bioequivalent or pharmaceutically acceptable salt thereof. Other preferred compds. are duloxetine and venlafaxine or a bioequivalent or pharmaceutically acceptable salt thereof. In yet another embodiment, a therapeutically effective amt. of a non-tricyclic triple reuptake inhibitor ('TRI') compd. of a specific type, or a pharmaceutically acceptable sait thereof, is administered. The TRI compds. are characterized by their ability to block the reuptake (and, hence, increase central concns. of) the three primary brain monoamines: serotonin, noradrenaline, and dopamine.

IT **92623-85-3D**, Milnacipran, deriv.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of depression secondary to pain using milnacipran and other monoamine reuptake inhibitors)

RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

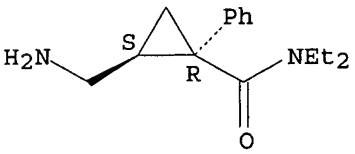
L42 ANSWER 10 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:971923 CAPLUS
DOCUMENT NUMBER: 140:8867
TITLE: Combination of atypical antipsychotic and serotonin reuptake inhibitor for the treatment of chronic pain
INVENTOR(S): Scheel-Krueger, Jorgen; Blackburn-Munro, Gordon John
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101492	A2	20031211	WO 2003-DK353	20030527
WO 2003101492	A3	20040129		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2002-833 A 20020530
ED Entered STN: 14 Dec 2003
AB This invention relates to the use of the combined action of an atypical antipsychotic and a serotonin reuptake inhibitor for the treatment of chronic pain.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of atypical antipsychotic and serotonin reuptake inhibitor for the treatment of chronic pain)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



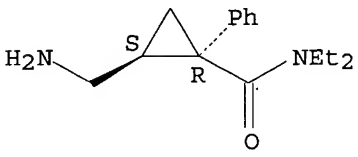
L42 ANSWER 11 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:875108 CAPLUS
DOCUMENT NUMBER: 139:333155
TITLE: Dual and triple reuptake inhibitors for the prevention and treatment of functional somatic disorders, including stress-related disorders
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090743	A1	20031106	WO 2003-US13247	20030424
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003232805	A1	20031218	US 2003-424212	20030424
PRIORITY APPLN. INFO.:			US 2002-375068P P	20020424
			US 2003-464288P P	20030418

ED Entered STN: 07 Nov 2003
AB Methods are provided for the prevention or treatment of stress-related disorders by administering a therapeutically effective amt. of a dual serotonin/norepinephrine reuptake inhibitor to an individual under stress. A triple monoamine reuptake inhibitor for serotonin/noradrenaline/dopamine may also be administered to an individual at risk for a stress-related disorder. In a preferred embodiment the compd. is milnacipran and is prophylactically administered at an effective amt. to delay or prevent stress-related disorders in an individual at risk.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dual and triple reuptake inhibitors for prevention and treatment of functional somatic disorders, including stress-related disorders)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

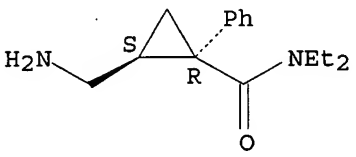
L42 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:757508 CAPLUS
DOCUMENT NUMBER: 139:255389
TITLE: Norepinephrine- and serotonin-reuptake inhibitors for treating visceral pain syndromes
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077897	A1	20030925	WO 2003-US8155	20030317
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003203055	A1	20031030	US 2003-391110	20030317
PRIORITY APPLN. INFO.:			US 2002-364531P P	20020315

OTHER SOURCE(S): MARPAT 139:255389
ED Entered STN: 26 Sep 2003
AB The invention provides a method for treating a visceral pain syndrome in a mammal. The method includes administering an effective amt. of a selective norepinephrine (NE)-serotonin (5-HT) reuptake inhibitor (NSRI), e.g., milnacipran.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(norepinephrine-serotonin reuptake inhibitors for treating visceral pain syndromes, and use with other agents)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:511137 CAPLUS
DOCUMENT NUMBER: 139:47219
TITLE: Methods of treating **fibromyalgia** syndrome, **chronic fatigue** syndrome and pain with dual serotonin-norepinephrine reuptake inhibitor
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

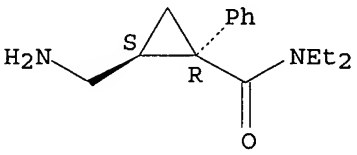
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053426	A1	20030703	WO 2002-US40976	20021219
W: CA, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
US 2003130353	A1	20030710	US 2001-28547	20011219
US 6602911	B2	20030805		

PRIORITY APPLN. INFO.: US 2001-28547 A1 20011219
US 2001-14149 A2 20011105

OTHER SOURCE(S): MARPAT 139:47219
ED Entered STN: 04 Jul 2003
AB The present invention provides a method of treating, in a mammal, chronic fatigue syndrome (CFS), chronic fatigue syndrome (CFS) that is assocd. with depression, a combination of chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS), fibromyalgia syndrome (FMS) assocd. with depression, pain, and pain assocd. with depression. The method includes administering a therapeutically effective amt. of a dual serotonin-norepinephrine reuptake inhibitor compd. or a pharmaceutically acceptable salt thereof.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of **fibromyalgia** and **chronic fatigue** syndrome and pain with dual serotonin-norepinephrine reuptake inhibitor)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



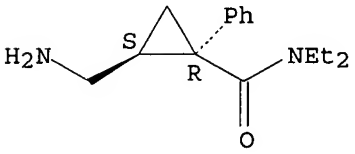
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:376684 CAPLUS
DOCUMENT NUMBER: 138:374216
TITLE: Selective norepinephrine serotonin reuptake inhibitors for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome and pain
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039598	A1	20030515	WO 2002-US35396	20021105
WO 2003039598	C1	20040603		
W: CA				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003139476	A1	20030724	US 2001-14149	20011105
US 6635675	B2	20031021		

PRIORITY APPLN. INFO.: US 2001-14149 A 20011105
OTHER SOURCE(S): MARPAT 138:374216
ED Entered STN: 16 May 2003
AB The present invention provides a method of treating, in a mammal, chronic fatigue syndrome (CFS), chronic fatigue syndrome (CFS) that is assocd. with depression, a combination of chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS), fibromyalgia syndrome (FMS) assocd. with depression, pain and pain assocd. with depression. The method includes administering a therapeutically effective amt. of a dual serotonin norepinepbrine reuptake inhibitor compd. or a pharmaceutically acceptable salt thereof. The effect of milnacipran in FMS animal and patients were examd.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective norepinephrine serotonin reuptake inhibitors for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome and pain)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

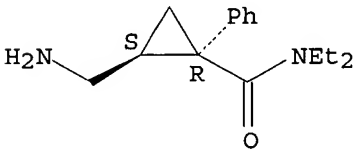
L42 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:521465 CAPLUS
DOCUMENT NUMBER: 137:98994
TITLE: Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics
INVENTOR(S): Wong, Erik Ho Fong; Gallen, Christopher C.; Svensson, Torgny
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA; Pharmacia AB
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053140	A2	20020711	WO 2001-US45871	20011227

WO 2002053140 A3 20021024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1353675 A2 20031022 EP 2001-991997 20011227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004517112 T2 20040610 JP 2002-554091 20011227
US 2002156067 A1 20021024 US 2001-35100 20011228
PRIORITY APPLN. INFO.: US 2001-259286P P 20010102
WO 2001-US45871 W 20011227

ED Entered STN: 12 Jul 2002
AB A compn. comprising: (a) a pharmaceutically effective amt. of one or more norepinephrine reuptake inhibitors or a salt; and (b) 1 or more neuroleptics is provided. The compn. is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating schizophrenia. A pharmaceutical compn. was prepd. by combining reboxetine with a neuroleptic in an acceptable carrier. The compn. contains 0.01-10 mg rebexetine and 25-300 mg clozapine.
IT **92623-85-3**, Milnacipran
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg. combination of norepinephrine reuptake inhibitors and neuroleptics)
RN 92623-85-3 CAPLUS
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:283758 CAPLUS
DOCUMENT NUMBER: 134:285613
TITLE: Treatment of fatigue, head injury and stroke with a selective noradrenaline reuptake inhibitor combined with phenylalanine or tyrosine
INVENTOR(S): Horrobin, David F.; Loder, Cari
PATENT ASSIGNEE(S): Laxdale Limited, UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001026623	A2	20010419	WO 2000-GB3926	20001012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2355191	A1	20010418	GB 1999-24172	19991012
EP 1220689	A2	20020710	EP 2000-969670	20001012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6441038	B1	20020827	US 2000-686629	20001012
NZ 518306	A	20040430	NZ 2000-518306	20001012
NO 2002001716	A	20020610	NO 2002-1716	20020411
PRIORITY APPLN. INFO.:			GB 1999-24172 A	19991012
			WO 2000-GB3926 W	20001012

ED Entered STN: 20 Apr 2001

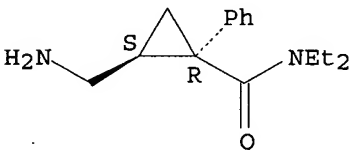
AB A method of treatment of disorders of neurol. origin and drug formulations for use in the method are disclosed. These conditions comprise fatigue and assocd. syndromes of pain, weakness and depressed mood which are assocd. with chronic fatigue syndrome, brain injury and stroke, stress, fibromyalgia, and irritable bowel syndrome. The treatment comprises administering to a patient in need thereof a selective inhibitor of noradrenaline reuptake combined with either phenylalanine or tyrosine in the same dosage form or the same pack. The noradrenergic drug may be selected from lofepramine, desipramine or reboxetine. The selective inhibitor may be a combined inhibitor of both noradrenaline and serotonin reuptake such as venlafaxine, duloxetine or milnacipran, or an inhibitor of both noradrenaline and dopamine reuptake such as bupropion.

IT **92623-85-3**, Milnacipran
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of fatigue, head injury and stroke with a selective noradrenaline reuptake inhibitor combined with phenylalanine or tyrosine)

RN 92623-85-3 CAPLUS

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 17 OF 44 USPATFULL on STN

ACCESSION NUMBER:	2004:139505 USPATFULL
TITLE:	Dosage escalation and divided daily dose of anti-depressants to treat neurological disorders
INVENTOR(S):	Rao, Srinivas G., San Diego, CA, UNITED STATES Kranzler, Jay D., LaJolla, CA, UNITED STATES Gendreau, R. Michael, Poway, CA, UNITED STATES
PATENT ASSIGNEE(S):	Cypress Bioscience, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004106681	A1	20040603
APPLICATION INFO.:	US 2003-678767	A1	20031003 (10)

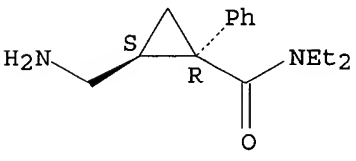
	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-415739P	20021003 (60)
	US 2002-431550P	20021206 (60)
	US 2003-443081P	20030128 (60)
	US 2003-443203P	20030128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1276
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method to treat neurological disorders. The method includes, e.g., administering higher daily dosages of anti-depressant. The higher daily dosages result in an improved efficacy of the drug, the maintenance of a positive patient toleration, the maintenance of a positive patient safety profile (e.g., dose limiting toxicity), a suitable peak plasma concentration (C.sub.max) of drug, and/or a once-a-day (QD) as opposed to twice-a-day (BID) administration. Applicant have discovered that increased daily dosages anti-depressant that would normally evoke adverse effects can be administered without the negative patient tolerability (i.e., adverse reactions) by escalating dosages over time. Such escalation dosages provide more efficacious amounts of anti-depressant than would otherwise be permitted. Similarly, higher levels of circulating drug are possible in patients by administering the compound in divided doses over the course of a day rather than once a day.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(dosage escalation and divided daily dose of antidepressants to treat neurol. disorders)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 18 OF 44 USPATFULL on STN
ACCESSION NUMBER: 2004:25274 USPATFULL
TITLE: Methods of treating fibromyalgia syndrome, chronic fatigue syndrome and pain
INVENTOR(S): Kranzler, Jay D., La Jolla, CA, UNITED STATES
Rao, Srinivas G., San Diego, CA, UNITED STATES

PATENT ASSIGNEE(S): Cypress Bioscience, Inc. (U.S. corporation)

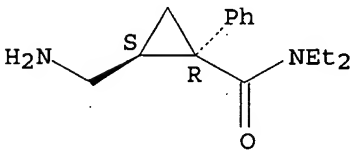
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004019116	A1	20040129
APPLICATION INFO.:	US 2003-623431	A1	20030718 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-28547, filed on 19 Dec 2001, GRANTED, Pat. No. US 6602911 Continuation-in-part of Ser. No. US 2001-14149, filed on 5 Nov 2001, GRANTED, Pat. No. US 6635675
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method of treating fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), and pain in an animal subject. The method generally involves administering a therapeutically effective amount of a dual serotonin norepinephrine reuptake inhibitor compound or a pharmaceutically acceptable salt thereof, wherein said dual serotonin norepinephrine reuptake inhibitor compound is characterized by a non-tricyclic structure and an equal or greater inhibition of norepinephrine reuptake than serotonin reuptake. In particular, the use of milnacipran to treat FMS, CFS, and pain is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(selective norepinephrine serotonin reuptake inhibitors for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome and pain)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 19 OF 44 USPATFULL on STN
ACCESSION NUMBER: 2003:330590 USPATFULL
TITLE: Prevention and treatment of functional somatic disorders, including stress-related disorders
INVENTOR(S): Kranzler, Jay D., LaJolla, CA, UNITED STATES
Rao, Srinivas G., San Diego, CA, UNITED STATES
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., San Diego, CA, UNITED STATES, 92131 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232805	A1	20031218

APPLICATION INFO.: US 2003-424212 A1 20030424 (10)

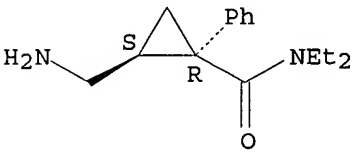
	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-375068P	20020424 (60)
	US 2003-464288P	20030418 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 1157
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for the prevention or treatment of stress-related disorders by administering a therapeutically effective amount of a dual serotonin/norepinephrine reuptake inhibitor to an individual under stress are described. A triple monoamine reuptake inhibitor for serotonin/noradrenaline/dopamine may also be administered to an individual at risk for a stress-related disorder. In a preferred embodiment the compound is milnacipran and is prophylactically administered at an effective amount to delay or prevent stress-related disorders in an individual at risk.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(dual and triple reuptake inhibitors for prevention and treatment of functional somatic disorders, including stress-related disorders)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 20 OF 44 USPATFULL on STN
ACCESSION NUMBER: 2003:288297 USPATFULL
TITLE: Methods of treating visceral pain syndromes
INVENTOR(S): Rao, Srinivas G., San Diego, CA, UNITED STATES
Kranzler, Jay D., La Jolla, CA, UNITED STATES
PATENT ASSIGNEE(S): Cypress Bioscience, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003203055	A1	20031030
APPLICATION INFO.:	US 2003-391110	A1	20030317 (10)

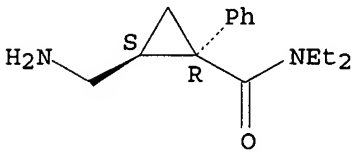
	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-364531P	20020315 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
NUMBER OF CLAIMS: 75
EXEMPLARY CLAIM: 1
LINE COUNT: 2838
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating a visceral pain syndromes in a mammal. The method includes administering to the mammal an effective amount of a selective norepinephrine (NE)-serotonin (5-HT) reuptake inhibitor (NSRI), e.g., milnacipran.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(norepinephrine-serotonin reuptake inhibitors for treating visceral pain syndromes, and use with other agents)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



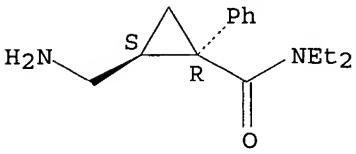
L42 ANSWER 21 OF 44 USPATFULL on STN
ACCESSION NUMBER: 2003:201489 USPATFULL
TITLE: METHOD OF TREATING CHRONIC FATIGUE SYNDROME
INVENTOR(S): Kranzler, Jay D., La Jolla, CA, UNITED STATES
Rao, Srinivas G., San Diego, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003139476	A1	20030724	
	US 6635675	B2	20031021	
APPLICATION INFO.:	US 2001-14149	A1	20011105	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), and pain in an animal subject comprising administering a therapeutically effective amount of a dual serotonin norepinephrine reuptake inhibitor compound or a pharmaceutically acceptable salt thereof, wherein said dual serotonin norepinephrine reuptake inhibitor compound is characterized by a non-tricyclic structure and a greater inhibition of norepinephrine reuptake than serotonin reuptake, and wherein said compound is not administered adjunctively with phenylalanine or tyrosine. In particular, the use of milnacipran to treat FMS, CFS, and pain is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(selective norepinephrine serotonin reuptake inhibitors for treating **fibromyalgia** syndrome, **chronic fatigue** syndrome and pain)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 22 OF 44 USPATFULL on STN

ACCESSION NUMBER:	2002:280621 USPATFULL		
TITLE:	New drug combinations		
INVENTOR(S):	Wong, Erik Ho Fong, Portage, MI, UNITED STATES Gallen, Christopher C., Wynnewood, PA, UNITED STATES Svensson, Torgny, Lidingo, SWEDEN		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002156067	A1	20021024
APPLICATION INFO.:	US 2001-35100	A1	20011228 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2001-259286P		20010102 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	PHARMACIA & UPJOHN, 301 HENRIETTA ST, 0228-32-LAW, KALAMAZOO, MI, 49007		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
LINE COUNT:	704		

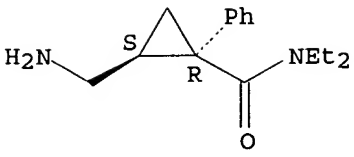
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A composition comprising:

(a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a pharmaceutically effective salt thereof; and

(b) a pharmaceutically effective amount of one or more neuroleptic agents or a pharmaceutically effective salt thereof is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating schizophrenia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **92623-85-3**, Milnacipran
(pharmaceuticals contg. combination of norepinephrine reuptake inhibitors and neuroleptics)
RN 92623-85-3 USPATFULL
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 23 OF 44 USPATFULL on STN

ACCESSION NUMBER:	2002:217310 USPATFULL		
TITLE:	Treatment of fatigue, head injury and stroke		
INVENTOR(S):	Loder, Cari, Farncombe, UNITED KINGDOM Horrobin, David F., Stirling, UNITED KINGDOM		
PATENT ASSIGNEE(S):	Laxdale Limited, Sterling, UNITED KINGDOM (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6441038	B1	20020827
APPLICATION INFO.:	US 2000-686629		20001012 (9)
	NUMBER		DATE
PRIORITY INFORMATION:	GB 1999-24172		19991012
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Cook, Rebecca		
LEGAL REPRESENTATIVE:	Foley & Lardner		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	602		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of treatment of disorders of neurological origin and drug formulations for use in the method are disclosed. These conditions comprise fatigue and associated syndromes of pain, weakness and depressed mood which are associated with chronic fatigue syndrome, brain injury and stroke, stress, fibromyalgia, and irritable bowel syndrome. The treatment comprises administering to a patient in need thereof a selective inhibitor of noradrenaline reuptake combined with either phenylalanine or tyrosine in the same dosage form or the same pack.#

The noradrenergic drug may be selected from lofepramine, desipramine or reboxetine. The selective inhibitor may be a combined inhibitor of both noradrenaline and serotonin reuptake such as venlafaxine, duloxetine or milnacipran, or an inhibitor of both noradrenaline and dopamine reuptake such as bupropion.

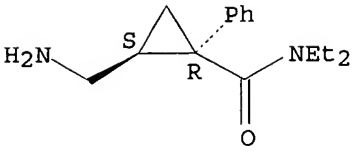
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **92623-85-3**, Milnacipran
(treatment of fatigue, head injury and stroke with a selective noradrenaline reuptake inhibitor combined with phenylalanine or tyrosine)

RN 92623-85-3 USPATFULL

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L42 ANSWER 24 OF 44 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004207034 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15105216
TITLE: The monoamine reuptake inhibitor milnacipran does not affect nociception to acute visceral distension in rats.
AUTHOR: Shin Sang-Wook; Eisenach James C; Rao Srinias G; Tong Chuanyao
CORPORATE SOURCE: Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA.
SOURCE: Anesthesia and analgesia, (2004 May) 98 (5) 1365-9, table of contents.
Journal code: 1310650. ISSN: 0003-2999.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040424
Last Updated on STN: 20040520
Entered Medline: 20040519

ABSTRACT:
The role of antidepressants in the treatment of visceral pain has not been extensively examined. Milnacipran, an antidepressant that inhibits monoamine reuptake, is widely used in the treatment of depression and fibromyalgia. In this study, we sought to determine the activity of milnacipran against acute visceral nociception. Female virgin rats were studied 7 days after bilateral ovariectomy. For uterine cervical distension (UCD), two metal rods were inserted into the cervical osses under general anesthesia for manual distension. Colorectal distension (CRD) was performed by insertion of a balloon catheter into the descending colon and rectum, followed by manual inflation. Two electrodes were inserted into the rectus abdominus muscle for recording UCD- or CRD-induced reflex contraction, which was quantified by electromyography (EMG). A dose response for milnacipran, administered intrathecally or i.v., was obtained for UCD and CRD stimulation. Milnacipran failed to inhibit the UCD-induced EMG response, whether administered i.v. or intrathecally. Similarly, i.v. milnacipran, administered either acutely or chronically, failed to inhibit the CRD-induced EMG response. CRD and UCD are well established animal models for the study of acute visceral pain. Milnacipran, although it provides some unique advantages compared with other antidepressants, is unlikely to produce analgesia after acute administration in the setting of acute visceral pain. IMPLICATIONS: Neither intrathecal nor i.v. milnacipran, a monoamine reuptake inhibitor, inhibits an acute visceral pain response induced by colorectal or uterine cervical distension.

CONTROLLED TERM: Check Tags: Female; Support, Non-U.S. Gov't
Adrenergic alpha-Agonists: PD, pharmacology
Animals
Balloon Dilatation
Clonidine: PD, pharmacology
Colon: PH, physiology

*Cyclopropanes: PD, pharmacology
Electromyography: DE, drug effects
Injections, Intravenous
Injections, Spinal
*Neurotransmitter Uptake Inhibitors: PD, pharmacology
Ovariectomy
***Pain: PP, physiopathology**
Physical Stimulation
Rats
Rats, Sprague-Dawley
Rectum: PH, physiology
Uterus: PH, physiology

Structures for hits from Medline & Embase printed on pages 65-67

CAS REGISTRY NO.: 4205-90-7 (Clonidine); **92623-85-3 (midalcipran)**
CHEMICAL NAME: 0 (Adrenergic alpha-Agonists); 0 (Cyclopropanes); 0 (Neurotransmitter Uptake Inhibitors)

L42 ANSWER 25 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004211092 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15108984
TITLE: Peripheral nerve injury sensitizes the response to visceral distension but not its inhibition by the antidepressant milnacipran.
COMMENT: Comment in: Anesthesiology. 2004 Mar;100(3):472-3. PubMed ID: 15108958
AUTHOR: Shin Sang-Wook; Eisenach James C
CORPORATE SOURCE: Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA.
CONTRACT NUMBER: GM48085 (NIGMS)
NS41386 (NINDS)
SOURCE: Anesthesiology, (2004 Mar) 100 (3) 671-5.
Journal code: 1300217. ISSN: 0003-3022.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040428
Last Updated on STN: 20040510
Entered Medline: 20040507

ABSTRACT:
BACKGROUND: Manipulations that cause hypersensitivity to visceral stimuli have been shown to also result in hypersensitivity to somatic stimuli coming from convergent dermatomes, but the converse has not been examined. The authors tested whether lumbar spinal nerve ligation in rats, a common model of neuropathic pain that results in hypersensitivity to somatic stimuli, also leads to hypersensitivity to visceral stimuli coming from convergent dermatomes and whether pharmacology of inhibition differed between these two sensory modalities. METHODS: Female Sprague-Dawley rats were anesthetized, and the left L5 and L6 spinal nerves were ligated. Animals received either intrathecal saline or milnacipran (0.1-3 microg), and withdrawal thresholds to mechanical testing in the left hind paw, using von Frey filaments, and visceral testing, using balloon colorectal distension, were determined. RESULTS: Nerve ligation resulted in decreases in threshold to withdrawal to somatic mechanical stimulation (from 13 +/- 1.8 g to 2.7 +/- 0.7 g) and also in decreases in threshold to reflex response to visceral stimulation (from 60 mmHg to 40 mmHg). Intrathecal milnacipran increased withdrawal threshold to somatic stimulation in a dose-dependent manner but failed to alter the response to noxious visceral stimulation. CONCLUSIONS: Injury of nerves innervating somatic structures enhances nociception from stimulation of viscera with convergent input from nearby dermatomes, suggesting that somatic neuropathic pain could be accompanied by an increased likelihood of visceral pain. Lack of efficacy of the antidepressant milnacipran against visceral stimuli suggests that visceral

hypersensitivity may not share the same pharmacology of inhibition as somatic hypersensitivity after nerve injury.
CONTROLLED TERM: Check Tags: Comparative Study; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amitriptyline: PD, pharmacology
Animals
*Antidepressive Agents: PD, pharmacology
Catheterization
*Cyclopropanes: PD, pharmacology
Dose-Response Relationship, Drug
Electromyography
Injections, Spinal
Ligation
***Pain: PP, physiopathology**
Pain Threshold: DE, drug effects
*Peripheral Nerves: IN, injuries
Physical Stimulation
Rats
Rats, Sprague-Dawley
Spinal Nerves: IN, injuries
Spinal Nerves: PA, pathology
CAS REGISTRY NO.: 50-48-6 (Amitriptyline); **92623-85-3 (midalcipran)**
CHEMICAL NAME: 0 (Antidepressive Agents); 0 (Cyclopropanes)

L42 ANSWER 26 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2003470177 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14533142
TITLE: Milnacipran for the treatment of chronic pain.
AUTHOR: Kamata Mitsuhiro; Naito Shingo; Takahashi Hitoshi; Higuchi Hisashi
SOURCE: Human psychopharmacology, (2003 Oct) 18 (7) 575-6. Journal code: 8702539. ISSN: 0885-6222.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031009
Last Updated on STN: 20031218
Entered Medline: 20031128
CONTROLLED TERM: Check Tags: Female; Human
Adrenergic Uptake Inhibitors: TU, therapeutic use
Aged
*Antidepressive Agents, Tricyclic: TU, therapeutic use
Chronic Disease
*Cyclopropanes: TU, therapeutic use
***Glossalgia: DT, drug therapy**
Serotonin Uptake Inhibitors: TU, therapeutic use
Treatment Outcome
CAS REGISTRY NO.: **92623-85-3 (midalcipran)**
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents, Tricyclic); 0 (Cyclopropanes); 0 (Serotonin Uptake Inhibitors)

L42 ANSWER 27 OF 44 MEDLINE on STN
ACCESSION NUMBER: 97081884 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8923127
TITLE: Efficacy and tolerability of milnacipran: an overview.
AUTHOR: Montgomery S A; Prost J F; Solles A; Briley M
CORPORATE SOURCE: St Mary's Hospital Medical School, London, UK.
SOURCE: International clinical psychopharmacology, (1996 Sep) 11

Suppl 4 47-51. Ref: 24
Journal code: 8609061. ISSN: 0268-1315.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319

ABSTRACT:
The relative benefits and risks of milnacipran, a novel antidepressant which selectively inhibits the reuptake of serotonin and noradrenaline, have been evaluated in comparative trials against tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs). A total of 2462 patients with major depressive disorders have been investigated. At the optimal dose (50 mg twice a day), the efficacy of milnacipran was equivalent to that of the TCAs, with response rates of approximately 65% in both cases. Milnacipran was consistently effective against all of the principal elements of depression (anxiety, cognitive function, sleep and psychomotor retardation), and did not produce sedation or the emergence of suicidal thoughts. The Clinical Global Impression (CGI-3) score, a measure of the overall therapeutic impact of a treatment, was significantly higher with milnacipran than with TCAs (1.98 versus 1.84, $p < 0.05$). TCAs were associated with a higher frequency of adverse events than milnacipran, particularly with respect to anticholinergic-like effects; dysuria was the only adverse event occurring twice as frequently with milnacipran than with TCAs. Compared with TCAs, milnacipran was also associated with a lower incidence of cardiovascular adverse events. No haematological abnormalities occurred during treatment with milnacipran, and the incidence of abnormal liver function tests tended to be lower with milnacipran than with TCAs. In comparisons with SSRIs, milnacipran produced significantly higher response rates. The CGI-3 scores were significantly higher in milnacipran-treated patients (2.64 versus 2.32, $p < 0.05$). The adverse event profiles of the two treatments were similar, as was the incidence of abnormal liver function tests. These studies suggest that milnacipran offers clinical advantages over TCAs in terms of tolerability, and over SSRIs in terms of efficacy. In particular, the lack of cardiovascular adverse events appears to offer advantages in cases of deliberate overdose. To date, 15 such overdoses have occurred; none was fatal and each had a favourable outcome. The reproducible pharmacokinetic characteristics of milnacipran present further advantages over both groups of agents, due to lack of drug accumulation and a low risk of drug interactions.

CONTROLLED TERM: Check Tags: Comparative Study; Human
Adrenergic Uptake Inhibitors: AE, adverse effects
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Antidepressive Agents: AE, adverse effects
*Antidepressive Agents: TU, therapeutic use
Antidepressive Agents, Tricyclic: TU, therapeutic use
Cyclopropanes: AE, adverse effects
*Cyclopropanes: TU, therapeutic use
*Depressive Disorder: DT, drug therapy
Headache: CI, chemically induced
Serotonin Uptake Inhibitors: AE, adverse effects
*Serotonin Uptake Inhibitors: TU, therapeutic use
CAS REGISTRY NO.: **92623-85-3 (midalcipran)**
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents); 0 (Antidepressive Agents, Tricyclic); 0 (Cyclopropanes); 0 (Serotonin Uptake Inhibitors)

L42 ANSWER 28 OF 44 MEDLINE on STN

ACCESSION NUMBER: 97081883 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8923126
TITLE: Milnacipran and selective serotonin reuptake inhibitors in major depression.
AUTHOR: Lopez-Ibor J; Guelfi J D; Pletan Y; Tournoux A; Prost J F
CORPORATE SOURCE: Neuva Zelanda 44, Madrid, Spain.
SOURCE: International clinical psychopharmacology, (1996 Sep) 11 Suppl 4 41-6. Ref: 32
Journal code: 8609061. ISSN: 0268-1315.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319

ABSTRACT:
In drug development the move from tricyclic antidepressants (TCAs) to selective serotonin reuptake inhibitors (SSRIs) involved not only the loss of the direct receptor interactions responsible for the adverse side effects of TCAs, but also the ability to inhibit the reuptake of noradrenaline. Selectivity for the single neurotransmitter, serotonin, may explain why SSRIs tend to be less efficacious than the TCAs, especially in more serious forms of depression. The advent of selective serotonin and noradrenaline reuptake inhibitors (SNRIs) has tended to confirm the idea that an action on both monoamine systems is important for maximal antidepressant efficacy. This paper reviews clinical trials comparing the new SNRI milnacipran with the SSRIs fluoxetine and fluvoxamine. A meta-analysis of the principal trials shows greater response rates (the proportion of patients with a decrease in symptom scores of 50% or more) with milnacipran (50 mg twice a day) than with fluoxetine (20 mg once a day), or fluvoxamine (100 mg twice a day) (milnacipran: 64%; SSRIs: 50%). Remission rates (the proportion of patients with Hamilton Depression Rating Scores of 7 or below) were also higher with milnacipran than with SSRIs (39 versus 28%). In one study, in which 100 mg milnacipran was given once a day in the evening, the higher response rate obtained with fluoxetine appears to be largely attributable to an inappropriate milnacipran dosage regimen. Data from a pharmacovigilance database including all patients participating in clinical trials with milnacipran (n = 5732) showed that, compared with the SSRIs, milnacipran produced fewer gastrointestinal side effects, such as nausea, and less anxiety. Milnacipran was, however, associated with a higher incidence of headache, dry mouth and dysuria. The results of these studies suggest that milnacipran is superior in efficacy to SSRIs and is equally well tolerated. Milnacipran, therefore, appears to offer a therapeutic advantage over the SSRIs.

CONTROLLED TERM: Check Tags: Comparative Study; Human
Adrenergic Uptake Inhibitors: AE, adverse effects
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Antidepressive Agents: AE, adverse effects
*Antidepressive Agents: TU, therapeutic use
Clinical Trials
Cyclopropanes: AE, adverse effects
*Cyclopropanes: TU, therapeutic use
*Depressive Disorder: DT, drug therapy
Headache: CI, chemically induced
Nausea: CI, chemically induced
Psychiatric Status Rating Scales
Serotonin Uptake Inhibitors: AE, adverse effects
*Serotonin Uptake Inhibitors: TU, therapeutic use
Treatment Outcome

CAS REGISTRY NO.: **92623-85-3 (midalcipran)**
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents); 0 (Cyclopropanes); 0 (Serotonin Uptake Inhibitors)

L42 ANSWER 29 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004379836 EMBASE
TITLE: Drug repositioning: Identifying and developing new uses for existing drugs.
AUTHOR: Ashburn T.T.; Thor K.B.
CORPORATE SOURCE: T.T. Ashburn, Dynogen Pharmaceuticals Inc., 31 St. James Avenue, Boston, MA 02116, United States. tashburn@dynogen.com
SOURCE: Nature Reviews Drug Discovery, (2004) 3/8 (673-683). Refs: 73
ISSN: 1474-1776 CODEN: NRDDAG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Biopharmaceutical companies attempting to increase productivity through novel discovery technologies have fallen short of achieving the desired results. Repositioning existing drugs for new indications could deliver the productivity increases that the industry needs while shifting the locus of production to biotechnology companies. More and more companies are scanning the existing pharmacopoeia for repositioning candidates, and the number of repositioning success stories is increasing.

CONTROLLED TERM: Medical Descriptors:
*drug research
drug industry
biotechnology
high throughput screening
attention deficit disorder: DT, drug therapy
overactive bladder: DT, drug therapy
hypertension: DT, drug therapy
hyperlipidemia: DT, drug therapy
economic aspect
depression: DT, drug therapy
drug mechanism
stress incontinence: DT, drug therapy
stress incontinence: SU, surgery
stress incontinence: TH, therapy
ejaculation disorder: SI, side effect
drug half life
smoking cessation
premature ejaculation: DT, drug therapy
fibromyalgia: DT, drug therapy
obesity: DT, drug therapy
Parkinson disease: DT, drug therapy
Alzheimer disease: DT, drug therapy
irritable colon: DT, drug therapy
osteoarthritis: DT, drug therapy
prostate hypertrophy: DT, drug therapy
hair loss: DT, drug therapy
erectile dysfunction: DT, drug therapy

epilepsy: DT, drug therapy
human
clinical trial
review
priority journal
Drug Descriptors:
methylphenidate: DT, drug therapy
oxybutynin: DT, drug therapy
oxybutynin: TD, transdermal drug administration
mevinolin: CB, drug combination
mevinolin: DT, drug therapy
nicotinic acid: CB, drug combination
nicotinic acid: DT, drug therapy
glibenclamide plus metformin: DT, drug therapy
amlodipine: CB, drug combination
amlodipine: DT, drug therapy
atorvastatin: CB, drug combination
atorvastatin: DT, drug therapy
duloxetine: DT, drug therapy
duloxetine: PD, pharmacology
fluoxetine: DT, drug therapy
fluoxetine: PD, pharmacology
serotonin: EC, endogenous compound
noradrenalin: EC, endogenous compound
dapoxetine: AE, adverse drug reaction
dapoxetine: CT, clinical trial
dapoxetine: DT, drug therapy
dapoxetine: PK, pharmacokinetics
dapoxetine: PD, pharmacology
amfebutamone: DT, drug therapy
amfebutamone: PD, pharmacology
milnacipran: CT, clinical trial
milnacipran: DT, drug therapy
milnacipran: PD, pharmacology
sibutramine: DT, drug therapy
sibutramine: PD, pharmacology
atomoxetine: DT, drug therapy
atomoxetine: PD, pharmacology
chlorpromazine: PD, pharmacology
galantamine: DT, drug therapy
galantamine: PD, pharmacology
acetylcholinesterase: EC, endogenous compound
ropinirole: CT, clinical trial
ropinirole: DT, drug therapy
ropinirole: PD, pharmacology
tofisopam: CT, clinical trial
tofisopam: DT, drug therapy
celecoxib: CT, clinical trial
celecoxib: DT, drug therapy
celecoxib: PD, pharmacology
cyclooxygenase 2: EC, endogenous compound
finasteride: DT, drug therapy
finasteride: PD, pharmacology
minoxidil: DT, drug therapy
minoxidil: PD, pharmacology
beta adrenergic receptor: EC, endogenous compound
tadalafil: DT, drug therapy
tadalafil: PD, pharmacology
sildenafil: DT, drug therapy
sildenafil: PD, pharmacology
topiramate: DT, drug therapy
topiramate: PD, pharmacology

unindexed drug
ditropan xl
lovastatin plus nicotinic acid
caduet
sibut
zepreve

CAS REGISTRY NO.: (methylphenidate) 113-45-1, 298-59-9; (oxybutynin) 1508-65-2, 5633-20-5; (mevinolin) 75330-75-5; (nicotinic acid) 54-86-4, 59-67-6; (amlodipine) 88150-42-9; (atorvastatin) 134523-00-5, 134523-03-8; (duloxetine) 116539-59-4, 136434-34-9; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (serotonin) 50-67-9; (noradrenalin) 1407-84-7, 51-41-2; (dapoxetine) 119356-77-3; (amfebutamone) 31677-93-7, 34911-55-2; (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (sibutramine) 106650-56-0; (atomoxetine) 82248-59-7, 82857-39-4, 82857-40-7, 83015-26-3; (chlorpromazine) 50-53-3, 69-09-0; (galantamine) 1953-04-4, 357-70-0; (acetylcholinesterase) 9000-81-1; (ropinirole) 91374-21-9; (tofisopam) 22345-47-7; (celecoxib) 169590-42-5; (finasteride) 98319-26-7; (minoxidil) 38304-91-5; (tadalafil) 171596-29-5; (sildenafil) 139755-83-2; (topiramate) 97240-79-4

CHEMICAL NAME: (1) Concerta; (2) Ditropan xl; (3) Oxytrol; (4) Advicor; (5) Glucovance; (6) Caduet; (7) Cymbalta; (8) Prozac; (9) Wellbutrin; (10) Zyban; (11) Sarafem; (12) Ixel; (13) Meridia; (14) Sibut; (15) Strattera; (16) Thorazine; (17) Thorazine; (18) Reminyl; (19) Nivalin; (20) Requip; (21) Zepreve; (22) Grandaxin; (23) Seriel; (24) Celebrex; (25) Propecia; (26) Rogaine; (27) Cialis; (28) Cialis; (29) Viagra; (30) Topamax

COMPANY NAME: (1) Alza; (3) Watson; (4) Kos; (5) Bristol Myers Squibb; (12) Fabre; (13) Abbott; (14) Boots; (16) Smith Kline and French; (17) Rhone Poulenc; (19) Sopharma; (21) Glaxo SmithKline; (23) Egis; (25) Merck; (27) Lilly; (28) Icos; (29) Pfizer; (30) Johnson and Johnson; Cypress; Vela; Pharmacia Upjohn; SmithKline Beecham

L42 ANSWER 30 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004316005 EMBASE
TITLE: The management of fibromyalgia.
AUTHOR: Rao S.G.; Clauw D.J.
CORPORATE SOURCE: S.G. Rao, Cypress Bioscience, 4350 Executive Dr., San Diego, CA 92121, United States. srao@cypressbio.com
SOURCE: Drugs of Today, (2004) 40/6 (539-554).
Refs: 110
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
Fibromyalgia is one of a number of overlapping functional somatic syndromes," including irritable bowel syndrome, tension headache, chronic idiopathic lower back pain, chronic fatigue syndrome and others. These conditions affect females more frequently than males and probably share common underlying neurobiological mechanisms, as well as frequent psychological, cognitive and behavioral comorbidities. Since the pain in these conditions is most likely "central" in origin, classes of drugs such as nonsteroidal antiinflammatory drugs (NSAIDs)

and opioids, which are quite effective for "peripheral" pain, are relatively ineffective for the pain seen in these syndromes. Instead, tricyclic and other classes of antidepressants, antiseizure drugs and a number of other neuroactive compounds seem to be more effective. In addition, nonpharmacological therapies such as aerobic exercise and cognitive behavioral therapy are quite effective and frequently underutilized in clinical practice.

CONTROLLED TERM: Medical Descriptors:
***fibromyalgia: DT, drug therapy**
*fibromyalgia: TH, therapy
irritable colon
tension headache
low back pain
chronic fatigue syndrome
comorbidity
exercise
cognitive therapy
behavior therapy
clinical practice
sleep disorder
analgesia
human
clinical trial
review
Drug Descriptors:
nonsteroid antiinflammatory agent: CT, clinical trial
nonsteroid antiinflammatory agent: DT, drug therapy
opiate: CT, clinical trial
opiate: DT, drug therapy
tricyclic antidepressant agent: CT, clinical trial
tricyclic antidepressant agent: DT, drug therapy
anticonvulsive agent: CT, clinical trial
anticonvulsive agent: DT, drug therapy
serotonin uptake inhibitor: CT, clinical trial
serotonin uptake inhibitor: CM, drug comparison
serotonin uptake inhibitor: DT, drug therapy
monoamine oxidase inhibitor: CT, clinical trial
monoamine oxidase inhibitor: DT, drug therapy
amitriptyline: CT, clinical trial
amitriptyline: CM, drug comparison
amitriptyline: DT, drug therapy
clomipramine: CT, clinical trial
clomipramine: DT, drug therapy
doxepin: CT, clinical trial
doxepin: DT, drug therapy
fluoxetine: CT, clinical trial
fluoxetine: CM, drug comparison
fluoxetine: DT, drug therapy
citalopram: CT, clinical trial
citalopram: DT, drug therapy
sertraline: CT, clinical trial
sertraline: DT, drug therapy
paroxetine: CT, clinical trial
paroxetine: CM, drug comparison
paroxetine: DT, drug therapy
venlafaxine: CT, clinical trial
venlafaxine: DT, drug therapy
milnacipran: CT, clinical trial
milnacipran: DT, drug therapy
moclobemide: CT, clinical trial
moclobemide: DT, drug therapy

pirlindole: CT, clinical trial
pirlindole: DT, drug therapy
ibuprofen: CT, clinical trial
ibuprofen: DT, drug therapy
naproxen: CT, clinical trial
naproxen: DT, drug therapy
pregabalin: CT, clinical trial
pregabalin: DT, drug therapy
zopiclone: CT, clinical trial
zopiclone: DT, drug therapy
zolpidem: DT, drug therapy
cyclobenzaprine: CT, clinical trial
cyclobenzaprine: DT, drug therapy
morphine: CT, clinical trial
morphine: DT, drug therapy
morphine: IV, intravenous drug administration
tramadol: CT, clinical trial
tramadol: DT, drug therapy
tropisetron: CT, clinical trial
tropisetron: DT, drug therapy
ketamine: CT, clinical trial
ketamine: DT, drug therapy
dextromethorphan: CT, clinical trial
dextromethorphan: DT, drug therapy
growth hormone: CT, clinical trial
growth hormone: DT, drug therapy

CAS REGISTRY NO.: (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (amitriptyline) 50-48-6, 549-18-8; (clomipramine) 17321-77-6, 303-49-1; (doxepin) 1229-29-4, 1668-19-5; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (citalopram) 59729-33-8; (sertraline) 79617-96-2; (paroxetine) 61869-08-7; (venlafaxine) 93413-69-5; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (moclobemide) 71320-77-9; (pirlindole) 16154-78-2, 60762-57-4; (ibuprofen) 15687-27-1; (naproxen) 22204-53-1, 26159-34-2; (pregabalin) 148553-50-8; (zopiclone) 43200-80-2; (zolpidem) 82626-48-0; (cyclobenzaprine) 303-53-7, 6202-23-9; (morphine) 52-26-6, 57-27-2; (tramadol) 27203-92-5, 36282-47-0; (tropisetron) 89565-68-4; (ketamine) 1867-66-9, 6740-88-1, 81771-21-3; (dextromethorphan) 125-69-9, 125-71-3; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6

L42 ANSWER 31 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004379137 EMBASE
TITLE: Milnacipran treatment of a terminally ill cancer patient with major depressive disorder [1].
AUTHOR: Sato K.; Higuchi H.; Yoshida K.; Takahashi H.; Shimizu T.; Watanabe J.
CORPORATE SOURCE: K. Sato, Division of Neuropsychiatry, Dept. of Neuro and Locomotor Science, Akita University School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan
SOURCE: Human Psychopharmacology, (2004) 19/6 (431-432).
Refs: 9
ISSN: 0885-6222 CODEN: HUPSEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
032 Psychiatry
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*cancer patient
*major depression: DI, diagnosis
*major depression: DT, drug therapy
terminal disease
comorbidity
lung cancer: DI, diagnosis
lung cancer: DT, drug therapy
dyspnea
cancer pain: DT, drug therapy
mood disorder
anxiety disorder
fatigue
anorexia
guilt
suicidal behavior
sleep disorder: DT, drug therapy
treatment outcome
symptomatology
side effect: SI, side effect
spine metastasis: CO, complication
convalescence
bronchopneumonia: CO, complication
death
human
male
case report
adult
letter
priority journal
Drug Descriptors:
*milnacipran: AE, adverse drug reaction
*milnacipran: DT, drug therapy
zolpidem: DT, drug therapy
trazodone: DT, drug therapy
antineoplastic agent: DT, drug therapy
morphine: DT, drug therapy
antacid agent: DT, drug therapy
laxative: DT, drug therapy
CAS REGISTRY NO.: (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (zolpidem) 82626-48-0; (trazodone) 19794-93-5, 25332-39-2; (morphine) 52-26-6, 57-27-2

L42 ANSWER 32 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004358375 EMBASE
TITLE: A case of temporo-mandibular disorder with fibromyalgia treated with the antidepressant, milnacipran [3].
AUTHOR: Toyofuku A.; Miyako H.
CORPORATE SOURCE: A. Toyofuku, Department of Dentistry/Oral Surgery, School of Medicine, Fukuoka University, 7-45-1 Nanakuma, Johan-ku, Fukuoka, Japan. toyofuku@minf.med.fukuoka-u.ac.jp
SOURCE: Human Psychopharmacology, (2004) 19/5 (357-358).
Refs: 6
ISSN: 0885-6222 CODEN: HUPSEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
011 Otorhinolaryngology

030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*temporomandibular joint disorder: CO, complication
*temporomandibular joint disorder: DI, diagnosis
*temporomandibular joint disorder: DT, drug therapy
*fibromyalgia: CO, complication
*fibromyalgia: DI, diagnosis
***fibromyalgia: DT, drug therapy**
comorbidity
treatment outcome
orthodontics
psychosomatic disorder: CO, complication
psychosomatic disorder: DT, drug therapy
fatigue: CO, complication
fatigue: SI, side effect
sleep disorder: CO, complication
headache: CO, complication
headache: DT, drug therapy
shoulder pain: CO, complication
shoulder pain: DT, drug therapy
backache: CO, complication
backache: DT, drug therapy
muscle stiffness
walking
depression: DI, diagnosis
depression: DT, drug therapy
diagnostic procedure
rating scale
disease exacerbation: SI, side effect
dose response
heart palpitation: SI, side effect
daily life activity
pain assessment
drug efficacy
sedation
side effect: SI, side effect
human
female
case report
adult
letter
priority journal
Drug Descriptors:
*milnacipran: AE, adverse drug reaction
*milnacipran: CB, drug combination
*milnacipran: DO, drug dose
*milnacipran: DT, drug therapy
*milnacipran: PD, pharmacology
antidepressant agent: AE, adverse drug reaction
antidepressant agent: CB, drug combination
antidepressant agent: DO, drug dose
antidepressant agent: DT, drug therapy
antidepressant agent: PD, pharmacology
fluvoxamine: CB, drug combination
fluvoxamine: DT, drug therapy
anxiolytic agent: CB, drug combination
anxiolytic agent: DT, drug therapy

alprazolam: CB, drug combination
alprazolam: DT, drug therapy
ethyl loflazepate: CB, drug combination
ethyl loflazepate: DT, drug therapy
amitriptyline: AE, adverse drug reaction
amitriptyline: DT, drug therapy
paroxetine: AE, adverse drug reaction
paroxetine: DT, drug therapy

CAS REGISTRY NO.: (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (fluvoxamine) 54739-18-3; (alprazolam) 28981-97-7; (ethyl loflazepate) 29177-84-2; (amitriptyline) 50-48-6, 549-18-8; (paroxetine) 61869-08-7

L42 ANSWER 33 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004359924 EMBASE
TITLE: An eye on the markets.
SOURCE: Current Drug Discovery, (2004) -/JULY (39-40).
ISSN: 1472-7463 CODEN: CDDUAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*fibromyalgia: DI, diagnosis
***fibromyalgia: DT, drug therapy**
*fibromyalgia: ET, etiology
prevalence
United States
diagnostic accuracy
symptomatology
weight gain
body weight disorder: SI, side effect
drowsiness: SI, side effect
dizziness: SI, side effect
heart arrhythmia: SI, side effect
xerostomia: SI, side effect
hypotension: SI, side effect
pathogenesis
medical research
side effect: SI, side effect
human
clinical trial
note
Drug Descriptors:
tricyclic antidepressant agent: AE, adverse drug reaction
tricyclic antidepressant agent: CM, drug comparison
tricyclic antidepressant agent: DT, drug therapy
antiinflammatory agent: DT, drug therapy
motifene: DT, drug therapy
milnacipran: AE, adverse drug reaction
milnacipran: CT, clinical trial
milnacipran: CM, drug comparison
milnacipran: DT, drug therapy
milnacipran: PD, pharmacology
pregabalin: AE, adverse drug reaction
pregabalin: CT, clinical trial
pregabalin: CM, drug comparison
pregabalin: DT, drug therapy

gabapentin
oxybate sodium: CT, clinical trial
oxybate sodium: DT, drug therapy
pindolol
amine
unclassified drug
lyrica

CAS REGISTRY NO.: (milnacipran) **101152-94-7, 86181-08-0,**
92623-85-3; (pregabalin) 148553-50-8; (gabapentin)
60142-96-3; (oxybate sodium) 502-85-2; (pindolol)
13523-86-9, 21870-06-4

CHEMICAL NAME: (1) Neurontin; Motifene; Lyrica

COMPANY NAME: (1) Pfizer; Fabre; Cypress; Orphan; Astra Zeneca

L42 ANSWER 34 OF 44 EMBASE
on STN

ACCESSION NUMBER: 2004226914 EMBASE

TITLE: [Fibromyalgia: State of the art].
FIBROMIALGIA: STATO DELL'ARTE.

AUTHOR: Fietta P.

CORPORATE SOURCE: Dr. P. Fietta, Unita Oper. di Reumatol. e Med. Int., Dipartimento Osteoarticolare, Azienda Ospedaliera di Parma, Via Gramsci 14, 43100 Parma, Italy. farnese15@libero.it

SOURCE: Minerva Medica, (2004) 95/1 (35-52).
Refs: 169
ISSN: 0026-4806 CODEN: MIMEAO

COUNTRY: Italy

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 008 Neurology and Neurosurgery
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: Italian; English

SUMMARY LANGUAGE: English; Italian

ABSTRACT:
Fibromyalgia (FM) is a common and complex condition, defined as long lasting, widespread musculoskeletal pain, in the presence of tender points (TPs) at specific anatomical sites. Dysautonomic and functional symptoms, such as orthostatic hypotension, tachycardia, effort intolerance, marked fatigue, sleep disorders, cognitive disturbances, psychological distress, paresthesias, headache, genitourinary manifestations, irritable bowel syndrome and bladder dyskinesia, frequently occur. The etiopathogenesis of FM is presently unknown, but nociceptor, autonomic and neuro-endocrine system dysfunctions have been found in patients. Since specific serological or instrumental markers of the syndrome are not yet identifiable, TP search is the only useful diagnostic hallmark. The development of an effective therapy of FM has hitherto been hampered by the incomplete knowledge of its pathogenic mechanisms. In this paper, the most recent information on FM is reviewed.

CONTROLLED TERM: Medical Descriptors:
*fibromyalgia: DI, diagnosis
***fibromyalgia: DT, drug therapy**
*fibromyalgia: EP, epidemiology
*fibromyalgia: ET, etiology
*fibromyalgia: RH, rehabilitation
*fibromyalgia: TH, therapy
chronic disease
symptomatology
orthostatic hypotension
tachycardia
exercise tolerance
fatigue

sleep disorder: SI, side effect
cognitive defect
distress syndrome
paresthesia
headache
urogenital tract disease
irritable colon
bladder dysfunction
pathogenesis
serology
diagnostic procedure
nociception
allodynia
hyperalgesia
side effect: SI, side effect
hangover: SI, side effect
xerostomia: SI, side effect
human
review
Drug Descriptors:
corticosteroid
opiate
nonsteroid antiinflammatory agent: CB, drug combination
nonsteroid antiinflammatory agent: CM, drug comparison
nonsteroid antiinflammatory agent: DT, drug therapy
paracetamol: CM, drug comparison
paracetamol: DT, drug therapy
tramadol: CB, drug combination
tramadol: DT, drug therapy
benzodiazepine derivative: AE, adverse drug reaction
benzodiazepine derivative: DT, drug therapy
zopiclone: DT, drug therapy
zolpidem: DT, drug therapy
4 hydroxybutyric acid: DT, drug therapy
clonazepam: DT, drug therapy
pregabalin: DT, drug therapy
melatonin: DT, drug therapy
cyclobenzaprine: AE, adverse drug reaction
cyclobenzaprine: CB, drug combination
cyclobenzaprine: DO, drug dose
cyclobenzaprine: DT, drug therapy
tizanidine: DT, drug therapy
pramipexole: DT, drug therapy
serotonin uptake inhibitor: CB, drug combination
serotonin uptake inhibitor: DT, drug therapy
tricyclic antidepressant agent: AE, adverse drug reaction
tricyclic antidepressant agent: DT, drug therapy
fluoxetine: CB, drug combination
fluoxetine: DT, drug therapy
amitriptyline: CB, drug combination
amitriptyline: DT, drug therapy
venlafaxine: DT, drug therapy
milnacipran: DT, drug therapy
sibutramine: DT, drug therapy
reboxetine: DT, drug therapy
antiemetic agent: DT, drug therapy
tropisetron: DT, drug therapy
s adenosylmethionine: AE, adverse drug reaction
s adenosylmethionine: DT, drug therapy
alpha interferon: DO, drug dose
alpha interferon: DT, drug therapy
growth hormone: DT, drug therapy

CAS REGISTRY NO.: (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (paracetamol) 103-90-2; (tramadol) 27203-92-5, 36282-47-0; (zopiclone) 43200-80-2; (zolpidem) 82626-48-0; (4 hydroxybutyric acid) 591-81-1; (clonazepam) 1622-61-3; (pregabalin) 148553-50-8; (melatonin) 73-31-4; (cyclobenzaprine) 303-53-7, 6202-23-9; (tizanidine) 51322-75-9, 64461-82-1; (pramipexole) 104632-26-0; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (amitriptyline) 50-48-6, 549-18-8; (venlafaxine) 93413-69-5; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (sibutramine) 106650-56-0; (reboxetine) 98769-81-4, 98769-84-7; (tropisetron) 89565-68-4; (s adenosylmethionine) 29908-03-0, 485-80-3; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6

L42 ANSWER 35 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004120926 EMBASE

TITLE: International Journal of Psychiatry in Clinical Practice: Editorial.

AUTHOR: Baldwin D.; Kasper S.

SOURCE: International Journal of Psychiatry in Clinical Practice, (2004) 8/1 (1).
ISSN: 1365-1501 CODEN: IJPCFZ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Editorial

FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*psychiatry
medical literature
clinical research
psychiatric diagnosis
schizophrenia: DT, drug therapy
prolactin blood level
depression: DI, diagnosis
somatoform disorder: DI, diagnosis
prescription
drug efficacy
drug tolerance
fibromyalgia: DT, drug therapy
comorbidity
posttraumatic stress disorder: DT, drug therapy
posttraumatic stress disorder: TH, therapy
physical examination
hospital admission
medical assessment
dysthymia: DT, drug therapy
dysthymia: TH, therapy
suicide
human
editorial
priority journal
Drug Descriptors:
neuroleptic agent: DT, drug therapy
risperidone: DT, drug therapy
prolactin: EC, endogenous compound
valproic acid: DT, drug therapy
oxcarbazepine: DT, drug therapy
milnacipran: DT, drug therapy

noradrenalin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: DT, drug therapy
paroxetine: DT, drug therapy
psychotropic agent: DT, drug therapy
CAS REGISTRY NO.: (risperidone) 106266-06-2; (prolactin) 12585-34-1, 50647-00-2, 9002-62-4; (valproic acid) 1069-66-5, 99-66-1; (oxcarbazepine) 28721-07-5; (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (paroxetine) 61869-08-7

L42 ANSWER 36 OF 44 EMBASE
on STN
ACCESSION NUMBER: 2003302940 EMBASE
TITLE: [Fibromyalgia: A challenge for neuroscience].
FIBROMIALGIA: UN RETO TAMBIEN PARA LA NEUROCIENCIA.
AUTHOR: Leza J.C.
CORPORATE SOURCE: Prof. J.C. Leza, Departamento de Farmacologia, Facultad de Medicina, Universidad Complutense, Ciudad Universitaria, E-28040 Madrid, Spain. jcleza@med.ucm.es
SOURCE: Revista de Neurologia, (16 Jul 2003) 36/12 (1165-1175).
Refs: 134
ISSN: 0210-0010 CODEN: RVNRAA
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: Spanish
SUMMARY LANGUAGE: English; Spanish; Portuguese
ABSTRACT:
Aims. In this survey we present the most recent findings regarding the physiopathology and therapeutic guidelines of a disease we still know very little about: fibromyalgia. This disorder is characterized by a chronic process of generalized musculoskeletal pain accompanied by chronic fatigue, sleep disorders and, on many occasions, neuroendocrine disorders. Development. Most research on the physiopathology of fibromyalgia points towards some kind of pain transmission disorder in the dorsal horn of the spinal cord. In chronic pain processes, a 'resonance' effect is produced in the synapse of the dorsal horn and this gives rise to allodynia and hyperalgesia. From a biochemical point of view, glutamate and substance P receptors, as well as the main systems involved in the transmission of pain, serotonin and noradrenaline, seem to play a fundamental role. Patients with fibromyalgia have generally been seen to have lowered 5HT activity and an increase in substance P. In addition to these alterations in the perception of pain, serotonin could also be responsible for the frequently occurring sleep, hormone and neuropsychiatric disorders observed in these patients. Conclusions. Nowadays fibromyalgia is still a challenge for modern medicine. Indeed, the neuroscientific community must design a basic scientific approach carried out at the patient's bedside in order to find pharmacological tools with which to relieve these symptoms. Of the extensive therapeutic arsenal that has been tested in these patients to date, classical antidepressants and serotonin and noradrenaline reuptake inhibitors, used in sub-antidepressant doses, seem to be the most effective.

CONTROLLED TERM: Medical Descriptors:
*fibromyalgia: DI, diagnosis
***fibromyalgia: DT, drug therapy**
*fibromyalgia: EP, epidemiology
*fibromyalgia: ET, etiology
chronic pain: ET, etiology
chronic fatigue syndrome: ET, etiology

neuropathic pain: ET, etiology
pathophysiology
prevalence
questionnaire
pain assessment
health status
rating scale
neurotransmission
inflammation
human
male
female
clinical trial
meta analysis
adolescent
child
adult
review
Drug Descriptors:
*tricyclic antidepressant agent: CT, clinical trial
*tricyclic antidepressant agent: DT, drug therapy
*tricyclic antidepressant agent: PD, pharmacology
*serotonin uptake inhibitor: DO, drug dose
*serotonin uptake inhibitor: DT, drug therapy
cytokine: EC, endogenous compound
interleukin 1beta: EC, endogenous compound
interleukin 6: EC, endogenous compound
tumor necrosis factor alpha: EC, endogenous compound
interleukin 8: EC, endogenous compound
prostaglandin E2: IM, intramuscular drug administration
antidepressant agent: CT, clinical trial
antidepressant agent: DO, drug dose
antidepressant agent: DT, drug therapy
antidepressant agent: PD, pharmacology
amitriptyline: CT, clinical trial
amitriptyline: DT, drug therapy
amitriptyline: PD, pharmacology
clomipramine: CT, clinical trial
clomipramine: DT, drug therapy
clomipramine: PD, pharmacology
doxepin: CT, clinical trial
doxepin: DT, drug therapy
doxepin: PD, pharmacology
fluoxetine: DO, drug dose
fluoxetine: DT, drug therapy
fluoxetine: PD, pharmacology
paroxetine: DO, drug dose
paroxetine: DT, drug therapy
paroxetine: PD, pharmacology
citalopram: DO, drug dose
citalopram: DT, drug therapy
citalopram: PD, pharmacology
venlafaxine: DT, drug therapy
venlafaxine: PD, pharmacology
mirtazapine: DT, drug therapy
mirtazapine: PD, pharmacology
reboxetine: DT, drug therapy
reboxetine: PD, pharmacology
nefazodone: DT, drug therapy
nefazodone: PD, pharmacology
duloxetine: DT, drug therapy
duloxetine: PD, pharmacology

milnacipran: DT, drug therapy
milnacipran: PD, pharmacology
monoamine oxidase inhibitor: DT, drug therapy
monoamine oxidase inhibitor: PD, pharmacology
phenelzine: DT, drug therapy
phenelzine: PD, pharmacology
tranylcypromine: DT, drug therapy
tranylcypromine: PD, pharmacology
moclobemide: DT, drug therapy
moclobemide: PD, pharmacology
anxiolytic agent: DT, drug therapy
hypnotic sedative agent: DT, drug therapy
benzodiazepine: DT, drug therapy
zopiclone: DT, drug therapy
unindexed drug

CAS REGISTRY NO.: (interleukin 8) 114308-91-7; (prostaglandin E2) 363-24-6; (amitriptyline) 50-48-6, 549-18-8; (clomipramine) 17321-77-6, 303-49-1; (doxepin) 1229-29-4, 1668-19-5; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (paroxetine) 61869-08-7; (citalopram) 59729-33-8; (venlafaxine) 93413-69-5; (mirtazapine) 61337-67-5; (reboxetine) 98769-81-4, 98769-84-7; (nefazodone) 82752-99-6, 83366-66-9; (duloxetine) 116539-59-4, 136434-34-9; (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (phenelzine) 156-51-4, 51-71-8; (tranylcypromine) 13492-01-8, 155-09-9, 54-97-7; (moclobemide) 71320-77-9; (benzodiazepine) 12794-10-4; (zopiclone) 43200-80-2

L42 ANSWER 37 OF 44 EMBASE on STN

ACCESSION NUMBER: 2003305185 EMBASE
TITLE: Fibromyalgia syndrome: An overview of potential drug targets.
AUTHOR: Briley M.; Moret C.
CORPORATE SOURCE: M. Briley, NeuroBiz Consulting and Commun., Les Grezes, La Verdarie, 81100 Castres, France. mike.briley@neurobiz.com
SOURCE: IDrugs, (1 Jul 2003) 6/7 (668-673).
Refs: 71
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
032 Psychiatry
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Fibromyalgia syndrome (FMS) is a chronic disease of widespread and debilitating pain. The cause of FMS is unknown and its risk factors are poorly understood. It occurs frequently in the general population where it is often co-morbid with other rheumatoid and pain disorders, and psychiatric disorders such as anxiety and depression, making diagnosis particularly difficult. Several types of drugs are used to treat FMS, but none are specifically approved for this indication. FMS appears to be strongly associated with depression or at least with some symptoms of depression, and antidepressants appear to be effective in the treatment of this disorder. The advent of new classes of antidepressants with fewer side effects than older drugs has suggested new avenues of therapy for patients diagnosed with FMS.

CONTROLLED TERM: Medical Descriptors:

***fibromyalgia: DT, drug therapy**
*fibromyalgia: DR, drug resistance
*fibromyalgia: ET, etiology
human
clinical trial
meta analysis
nonhuman
chronic pain: DT, drug therapy
chronic pain: ET, etiology
risk factor
comorbidity
population
rheumatoid arthritis
mental disease
anxiety
depression: DT, drug therapy
drug approval
treatment indication
disease association
side effect: SI, side effect
pathophysiology
perception
nociception
postsynaptic membrane
drug activity
treatment failure
low back pain: DT, drug therapy
drug megadose
sleep disorder: DT, drug therapy
disease severity
review

Drug Descriptors:
antidepressant agent: DT, drug therapy
antidepressant agent: PD, pharmacology
antidepressant agent: AE, adverse drug reaction
serotonin 3 antagonist: DT, drug therapy
serotonin 3 antagonist: CT, clinical trial
neurokinin 1 receptor antagonist: DT, drug therapy
neurokinin 1 receptor antagonist: PD, pharmacology
duloxetine: DT, drug therapy
duloxetine: CB, drug combination
duloxetine: CM, drug comparison
milnacipran: DT, drug therapy
milnacipran: CM, drug comparison
milnacipran: PD, pharmacology
milnacipran: CT, clinical trial
milnacipran: DO, drug dose
venlafaxine: DT, drug therapy
venlafaxine: CM, drug comparison
venlafaxine: CT, clinical trial
venlafaxine: PD, pharmacology
venlafaxine: DO, drug dose
paroxetine: DT, drug therapy
paroxetine: CM, drug comparison
maprotiline: DT, drug therapy
maprotiline: CM, drug comparison
nortriptyline: DT, drug therapy
nortriptyline: CM, drug comparison
nortriptyline: PD, pharmacology
reboxetine: DT, drug therapy

reboxetine: CT, clinical trial
reboxetine: PD, pharmacology
citalopram: DT, drug therapy
citalopram: CM, drug comparison
citalopram: PD, pharmacology
citalopram: CB, drug combination
sertraline: DT, drug therapy
sertraline: CM, drug comparison
sertraline: PD, pharmacology
sertraline: CB, drug combination
fluoxetine: DT, drug therapy
fluoxetine: CM, drug comparison
fluoxetine: PD, pharmacology
fluoxetine: CB, drug combination
pirlindole: DT, drug therapy
pirlindole: CT, clinical trial
pirlindole: AE, adverse drug reaction
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: CB, drug combination
nonsteroid antiinflammatory agent: PD, pharmacology
paracetamol: DT, drug therapy
paracetamol: CB, drug combination
paracetamol: PD, pharmacology
tramadol: DT, drug therapy
tramadol: PD, pharmacology
opiate agonist: DT, drug therapy
opiate agonist: PD, pharmacology
pregabalin: DT, drug therapy
pregabalin: CT, clinical trial
tizanidine: DT, drug therapy
tizanidine: PD, pharmacology
tizanidine: CB, drug combination
baclofen: DT, drug therapy
baclofen: PD, pharmacology
baclofen: CB, drug combination
benzodiazepine derivative: DT, drug therapy
benzodiazepine derivative: PD, pharmacology
zopiclone: DT, drug therapy
zopiclone: PD, pharmacology
zopiclone: CB, drug combination
zolpidem: DT, drug therapy
zolpidem: PD, pharmacology
zolpidem: CB, drug combination
ketamine: DT, drug therapy
ketamine: DO, drug dose
ketamine: AE, adverse drug reaction
tropisetron: DT, drug therapy
tropisetron: CT, clinical trial
amitriptyline: DT, drug therapy
amitriptyline: CT, clinical trial
amitriptyline: AE, adverse drug reaction
amitriptyline: CM, drug comparison
amitriptyline: CB, drug combination
doxepin: DT, drug therapy
doxepin: CT, clinical trial
doxepin: AE, adverse drug reaction
doxepin: CM, drug comparison
doxepin: CB, drug combination
cyclobenzaprine: DT, drug therapy
cyclobenzaprine: CT, clinical trial
cyclobenzaprine: AE, adverse drug reaction
cyclobenzaprine: CM, drug comparison

cyclobenzaprine: CB, drug combination
unindexed drug
CAS REGISTRY NO.: (duloxetine) 116539-59-4, 136434-34-9; (milnacipran) **101152-94-7, 86181-08-0**; **92623-85-3**; (venlafaxine) 93413-69-5; (paroxetine) 61869-08-7; (maprotiline) 10262-69-8, 10347-81-6; (nortriptyline) 72-69-5, 894-71-3; (reboxetine) 98769-81-4, 98769-84-7; (citalopram) 59729-33-8; (sertraline) 79617-96-2; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (pirlindole) 16154-78-2, 60762-57-4; (paracetamol) 103-90-2; (tramadol) 27203-92-5, 36282-47-0; (pregabalin) 148553-50-8; (tizanidine) 51322-75-9, 64461-82-1; (baclofen) 1134-47-0; (zopiclone) 43200-80-2; (zolpidem) 82626-48-0; (ketamine) 1867-66-9, 6740-88-1, 81771-21-3; (tropisetron) 89565-68-4; (amitriptyline) 50-48-6, 549-18-8; (doxepin) 1229-29-4, 1668-19-5; (cyclobenzaprine) 303-53-7, 6202-23-9
COMPANY NAME: Pfizer; Sepracor

L42 ANSWER 38 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003291131 EMBASE
TITLE: Pharmacological therapies in fibromylagia.
AUTHOR: Rao S.G.; Bennett R.M.
CORPORATE SOURCE: S.G. Rao, Cypress Bioscience, Suite 325, 4350 Executive Drive, San Diego, CA 92121, United States. srao@cypressbio.com
SOURCE: Bailliere's Best Practice and Research in Clinical Rheumatology, (2003) 17/4 (611-627). Refs: 54
ISSN: 1521-6942 CODEN: BBPRFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
038 Adverse Reactions Titles
036 Health Policy, Economics and Management
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The fibromyalgia syndrome (FMS) is a common, chronic, widespread pain disorder that mainly affects middle-aged women. In addition to pain complaints, fatigue and disturbed sleep are symptoms frequently reported by these patients. Many FMS patients also meet diagnostic criteria for mood disorders (e.g. depression) as well as other so-called 'functional somatic syndromes', including irritable bowel syndrome, temporomandibular joint disorder, and subsets of chronic low-back pain. A wide variety of medications are used to manage the eclectic symptomatology of FMS patients, although relatively few have been rigorously tested. This chapter provides a contemporary update of the state of FMS pharmacotherapy, with an emphasis on compounds that have been tested in double-blind, randomized, controlled trials. Particular attention is paid to the efficacy of these therapies on the associated symptoms and co-morbid syndromes commonly seen in FMS patients.

CONTROLLED TERM: Medical Descriptors:
***fibromyalgia: DT, drug therapy**
*fibromyalgia: DM, disease management
human
controlled study
clinical trial

double blind procedure
randomized controlled trial
chronic disease: DT, drug therapy
chronic disease: DM, disease management
fatigue: DT, drug therapy
pain: DT, drug therapy
sleep disorder: DT, drug therapy
clinical feature
mood disorder: DT, drug therapy
depression: DT, drug therapy
irritable colon: DT, drug therapy
temporomandibular joint disorder: DT, drug therapy
low back pain: DT, drug therapy
restless legs syndrome: DT, drug therapy
headache: SI, side effect
chronic fatigue syndrome
multiple chemical sensitivity
pelvis pain syndrome
interstitial cystitis
symptomatology
drug efficacy
comorbidity
anticholinergic effect
side effect: SI, side effect
dose response
drug effect
Sjoegren syndrome: SI, side effect
weight gain
hangover: SI, side effect
drug potentiation
headache: DT, drug therapy
headache: PC, prevention
xerostomia: SI, side effect
gamma glutamyl transferase blood level
withdrawal syndrome: SI, side effect
cognitive defect: SI, side effect
drug fatality: SI, side effect
drug cost
quality of life
drug selectivity
drug tolerability
drug contraindication
migraine: DT, drug therapy
migraine: PC, prevention
food drug interaction
ileus: SI, side effect
review
priority journal
Drug Descriptors:
antidepressant agent: DT, drug therapy
antidepressant agent: CT, clinical trial
antidepressant agent: PD, pharmacology
antidepressant agent: AE, adverse drug reaction
antidepressant agent: DO, drug dose
antidepressant agent: CM, drug comparison
antidepressant agent: CB, drug combination
antidepressant agent: IT, drug interaction
tricyclic antidepressant agent: DT, drug therapy
tricyclic antidepressant agent: CT, clinical trial
tricyclic antidepressant agent: PD, pharmacology
tricyclic antidepressant agent: AE, adverse drug reaction
tricyclic antidepressant agent: DO, drug dose

tricyclic antidepressant agent: CM, drug comparison
tricyclic antidepressant agent: CB, drug combination
tricyclic antidepressant agent: IT, drug interaction
serotonin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: CT, clinical trial
serotonin uptake inhibitor: PD, pharmacology
serotonin uptake inhibitor: AE, adverse drug reaction
serotonin uptake inhibitor: CM, drug comparison
serotonin uptake inhibitor: CB, drug combination
serotonin uptake inhibitor: IT, drug interaction
serotonin uptake inhibitor: DO, drug dose
serotonin uptake inhibitor: PO, oral drug administration
monoamine oxidase inhibitor: DT, drug therapy
monoamine oxidase inhibitor: CT, clinical trial
monoamine oxidase inhibitor: PD, pharmacology
monoamine oxidase inhibitor: CM, drug comparison
monoamine oxidase inhibitor: CB, drug combination
monoamine oxidase inhibitor: IT, drug interaction
monoamine oxidase inhibitor: TD, transdermal drug administration
monoamine oxidase inhibitor: AE, adverse drug reaction
anticonvulsive agent: DT, drug therapy
anticonvulsive agent: PD, pharmacology
anticonvulsive agent: CT, clinical trial
anticonvulsive agent: CM, drug comparison
amitriptyline: DT, drug therapy
amitriptyline: CT, clinical trial
amitriptyline: PD, pharmacology
amitriptyline: DO, drug dose
amitriptyline: AE, adverse drug reaction
amitriptyline: CM, drug comparison
fluoxetine: DT, drug therapy
fluoxetine: CT, clinical trial
fluoxetine: PD, pharmacology
fluoxetine: CM, drug comparison
fluoxetine: CB, drug combination
fluoxetine: IT, drug interaction
citalopram: DT, drug therapy
citalopram: CT, clinical trial
citalopram: PD, pharmacology
citalopram: CM, drug comparison
sertraline: DT, drug therapy
sertraline: CT, clinical trial
sertraline: PD, pharmacology
sertraline: CM, drug comparison
noradrenalin uptake inhibitor: DT, drug therapy
noradrenalin uptake inhibitor: CM, drug comparison
noradrenalin uptake inhibitor: PD, pharmacology
noradrenalin uptake inhibitor: CT, clinical trial
noradrenalin uptake inhibitor: AE, adverse drug reaction
noradrenalin uptake inhibitor: DO, drug dose
noradrenalin uptake inhibitor: PO, oral drug administration
venlafaxine: DT, drug therapy
venlafaxine: PD, pharmacology
venlafaxine: CT, clinical trial
venlafaxine: DO, drug dose
venlafaxine: PO, oral drug administration
venlafaxine: CM, drug comparison
milnacipran: DT, drug therapy
milnacipran: CM, drug comparison
milnacipran: PD, pharmacology
milnacipran: CT, clinical trial

duloxetine: DT, drug therapy
duloxetine: PD, pharmacology
duloxetine: CM, drug comparison
phenelzine: DT, drug therapy
phenelzine: CB, drug combination
phenelzine: IT, drug interaction
phenelzine: TD, transdermal drug administration
phenelzine: AE, adverse drug reaction
tranylcypromine: DT, drug therapy
tranylcypromine: CB, drug combination
tranylcypromine: IT, drug interaction
tranylcypromine: TD, transdermal drug administration
tranylcypromine: AE, adverse drug reaction
pirlindole: DT, drug therapy
pirlindole: PD, pharmacology
pirlindole: CT, clinical trial
pirlindole: CM, drug comparison
moclobemide: DT, drug therapy
moclobemide: PD, pharmacology
moclobemide: CT, clinical trial
moclobemide: CM, drug comparison
reboxetine: DT, drug therapy
reboxetine: CT, clinical trial
reboxetine: PD, pharmacology
alosetron: DT, drug therapy
alosetron: CT, clinical trial
alosetron: PD, pharmacology
alosetron: AE, adverse drug reaction
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: PD, pharmacology
nonsteroid antiinflammatory agent: CB, drug combination
nonsteroid antiinflammatory agent: AE, adverse drug reaction
nonsteroid antiinflammatory agent: CT, clinical trial
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: CT, clinical trial
n methyl dextro aspartic acid receptor blocking agent: DO, drug dose
n methyl dextro aspartic acid receptor blocking agent: AE, adverse drug reaction
growth hormone: DT, drug therapy
growth hormone: CT, clinical trial
growth hormone: PD, pharmacology
growth hormone: PE, pharmacoeconomics
pregabalin: DT, drug therapy
pregabalin: CT, clinical trial
pregabalin: PD, pharmacology
pregabalin: CM, drug comparison
gabapentin: DT, drug therapy
gabapentin: PD, pharmacology
gabapentin: CM, drug comparison
hypnotic sedative agent: DT, drug therapy
hypnotic sedative agent: PD, pharmacology
hypnotic sedative agent: DO, drug dose
hypnotic sedative agent: CB, drug combination
muscle relaxant agent: DT, drug therapy
muscle relaxant agent: PD, pharmacology
muscle relaxant agent: CM, drug comparison

muscle relaxant agent: CB, drug combination
muscle relaxant agent: IT, drug interaction
muscle relaxant agent: AE, adverse drug reaction
muscle relaxant agent: DO, drug dose
muscle relaxant agent: CT, clinical trial
opiate derivative: DT, drug therapy
opiate derivative: PD, pharmacology
opiate derivative: AE, adverse drug reaction
opiate derivative: CT, clinical trial
opiate derivative: IV, intravenous drug administration
opiate derivative: CB, drug combination
opiate derivative: DO, drug dose
opiate derivative: PO, oral drug administration
opiate derivative: CM, drug comparison
serotonin 3 antagonist: DT, drug therapy
serotonin 3 antagonist: CT, clinical trial
serotonin 3 antagonist: PD, pharmacology
serotonin 3 antagonist: DO, drug dose
serotonin 3 antagonist: AE, adverse drug reaction
cyclobenzaprine: DT, drug therapy
cyclobenzaprine: CB, drug combination
cyclobenzaprine: IT, drug interaction
cyclobenzaprine: CT, clinical trial
cyclobenzaprine: PD, pharmacology
cyclobenzaprine: AE, adverse drug reaction
cyclobenzaprine: DO, drug dose
unindexed drug
paracetamol plus tramadol

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (citalopram) 59729-33-8; (sertraline) 79617-96-2; (venlafaxine) 93413-69-5; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (duloxetine) 116539-59-4, 136434-34-9; (phenelzine) 156-51-4, 51-71-8; (tranylcypromine) 13492-01-8, 155-09-9, 54-97-7; (pirlindole) 16154-78-2, 60762-57-4; (moclobemide) 71320-77-9; (reboxetine) 98769-81-4, 98769-84-7; (alosetron) 122852-42-0; (growth hormone) 36992-73-1, 37267-05-3, 66419-50-9, 9002-72-6; (pregabalin) 148553-50-8; (gabapentin) 60142-96-3; (muscle relaxant agent) 9008-44-0; (cyclobenzaprine) 303-53-7, 6202-23-9

CHEMICAL NAME: Lotronex; Ultracet

L42 ANSWER 39 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003420254 EMBASE
TITLE: Milnacipran for the treatment of chronic pain [2].
AUTHOR: Kamata M.; Naito S.; Takahashi H.; Higuchi H.
CORPORATE SOURCE: M. Kamata, Department of Psychiatry, Yuri Kumiai General Hospital, 38 Aza-Yago, Kawaguchi, Honjo City, Akita 015-8511, Japan
SOURCE: Human Psychopharmacology, (2003) 18/7 (575-576).
Refs: 8
ISSN: 0885-6222 CODEN: HUPSEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 008 Neurology and Neurosurgery
011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*chronic pain: DI, diagnosis
***chronic pain: DT, drug therapy**
*tongue disease: DI, diagnosis
*tongue disease: DT, drug therapy
eating disorder
consultation
otorhinolaryngology
medical specialist
insomnia: DT, drug therapy
treatment failure
drug withdrawal
treatment outcome
drug tolerability
human
female
case report
letter
priority journal
Drug Descriptors:
*milnacipran: DT, drug therapy
*milnacipran: PD, pharmacology
tricyclic antidepressant agent: DT, drug therapy
tricyclic antidepressant agent: PD, pharmacology
vitamin: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
triazolam: DT, drug therapy
diazepam: DT, drug therapy
antidepressant agent: DT, drug therapy
antidepressant agent: PD, pharmacology
venlafaxine
CAS REGISTRY NO.: (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**; (triazolam) 28911-01-5; (diazepam) 439-14-5; (venlafaxine) 93413-69-5

L42 ANSWER 40 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003172190 EMBASE
TITLE: Emerging trends in the pharmacotherapy of chronic pain.
AUTHOR: Nitu A.; Wallihan R.; Skljarevski V.; Ramadan N.M.
CORPORATE SOURCE: N.M. Ramadan, Eli Lilly and Co., Finch University of Health Sciences, Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064-3095, United States. ramadan@finchcms.edu
SOURCE: Expert Opinion on Investigational Drugs, (1 Apr 2003) 12/4 (545-559).
Refs: 100
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The pharmacotherapy for pain is dominated by conventional analgesics such as the opioids and the non-steroidal anti-inflammatory drugs. Recent advances in the understanding of the mechanisms of pain in general and chronic pain in particular, opened the field of analgesic therapy to newer pharmacological targets, which are aimed at improved efficacy and enhanced tolerability over

conventional antipain treatments. Many novel targets are still in preclinical development, but some have made it into human trials and have shown promise. Newer anticonvulsants, new generation cyclooxygenase inhibitors, better tolerated glutamate modulators and balanced serotonin/ noradrenaline re-uptake inhibitors are some targets that have shown promise in the clinic. These and other compounds that are in advanced phases of development for chronic pain are reviewed in this paper. It is hoped that the decade of pain control and research will lead us to an arsenal of effective and safe analgesics that will conquer the problem of chronic pain.

CONTROLLED TERM: Medical Descriptors:
***chronic pain: DT, drug therapy**
drug targeting
drug efficacy
drug tolerability
pain assessment
disease control
medical research
drug safety
drug mechanism
abdominal pain: SI, side effect
vertigo: SI, side effect
headache: SI, side effect
nausea and vomiting: SI, side effect
pharyngitis: SI, side effect
arthralgia: SI, side effect
dermatitis: SI, side effect
ecchymosis: SI, side effect
pain: SI, side effect
rash: SI, side effect
tinnitus: SI, side effect
gastrointestinal disease: SI, side effect
liver disease: SI, side effect
nystagmus: SI, side effect
fever: SI, side effect
apnea: SI, side effect
hypertension: SI, side effect
somnolence: SI, side effect
confusion: SI, side effect
hallucination: SI, side effect
dysmetria: SI, side effect
diarrhea: SI, side effect
respiratory tract disease: SI, side effect
thorax pain: SI, side effect
body weight disorder: SI, side effect
dysmenorrhea: SI, side effect
paresthesia: SI, side effect
speech disorder: SI, side effect
visual disorder: SI, side effect
fatigue: SI, side effect
xerostomia: SI, side effect
human
controlled study
review
Drug Descriptors:
*analgesic agent: AE, adverse drug reaction
*analgesic agent: DV, drug development
*analgesic agent: DT, drug therapy
*analgesic agent: PD, pharmacology
opiate: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
anticonvulsive agent: AE, adverse drug reaction

anticonvulsive agent: DV, drug development
anticonvulsive agent: DT, drug therapy
anticonvulsive agent: PD, pharmacology
prostaglandin synthase inhibitor: AE, adverse drug reaction
prostaglandin synthase inhibitor: DV, drug development
prostaglandin synthase inhibitor: DT, drug therapy
prostaglandin synthase inhibitor: PD, pharmacology
glutamate receptor antagonist: AE, adverse drug reaction
glutamate receptor antagonist: DV, drug development
glutamate receptor antagonist: DT, drug therapy
glutamate receptor antagonist: PD, pharmacology
serotonin uptake inhibitor: AE, adverse drug reaction
serotonin uptake inhibitor: DV, drug development
serotonin uptake inhibitor: DT, drug therapy
parecoxib: AE, adverse drug reaction
parecoxib: DV, drug development
parecoxib: DT, drug therapy
parecoxib: PD, pharmacology
cyclooxygenase 2 inhibitor: AE, adverse drug reaction
cyclooxygenase 2 inhibitor: DV, drug development
cyclooxygenase 2 inhibitor: DT, drug therapy
cyclooxygenase 2 inhibitor: PD, pharmacology
valdecoxib: AE, adverse drug reaction
valdecoxib: DV, drug development
valdecoxib: DT, drug therapy
valdecoxib: PD, pharmacology
etoricoxib: AE, adverse drug reaction
etoricoxib: DV, drug development
etoricoxib: DT, drug therapy
etoricoxib: PD, pharmacology
cyclooxygenase 1 inhibitor: AE, adverse drug reaction
cyclooxygenase 1 inhibitor: DV, drug development
cyclooxygenase 1 inhibitor: DT, drug therapy
cyclooxygenase 1 inhibitor: PD, pharmacology
licofelone: AE, adverse drug reaction
licofelone: DV, drug development
licofelone: DT, drug therapy
licofelone: PD, pharmacology
lumiracoxib: AE, adverse drug reaction
lumiracoxib: DV, drug development
lumiracoxib: DT, drug therapy
lumiracoxib: PD, pharmacology
zileuton: AE, adverse drug reaction
zileuton: DV, drug development
zileuton: DT, drug therapy
zileuton: PD, pharmacology
lamotrigine: AE, adverse drug reaction
lamotrigine: DV, drug development
lamotrigine: DT, drug therapy
lamotrigine: PD, pharmacology
oxcarbazepine: AE, adverse drug reaction
oxcarbazepine: DV, drug development
oxcarbazepine: DT, drug therapy
oxcarbazepine: PD, pharmacology
tetrodotoxin: AE, adverse drug reaction
tetrodotoxin: DV, drug development
tetrodotoxin: DT, drug therapy
tetrodotoxin: PD, pharmacology
topiramate: AE, adverse drug reaction
topiramate: DV, drug development
topiramate: DT, drug therapy
topiramate: PD, pharmacology

placebo
pregabalin: AE, adverse drug reaction
pregabalin: DV, drug development
pregabalin: DT, drug therapy
pregabalin: PD, pharmacology
dextromethorphan: AE, adverse drug reaction
dextromethorphan: DV, drug development
dextromethorphan: DT, drug therapy
dextromethorphan: PD, pharmacology
morphine: AE, adverse drug reaction
morphine: DV, drug development
morphine: DT, drug therapy
morphine: PD, pharmacology
memantine: AE, adverse drug reaction
memantine: DV, drug development
memantine: DT, drug therapy
memantine: PD, pharmacology
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3
isoquinolinecarboxylic acid: AE, adverse drug reaction
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3
isoquinolinecarboxylic acid: DV, drug development
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3
isoquinolinecarboxylic acid: DT, drug therapy
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3
isoquinolinecarboxylic acid: PD, pharmacology
milnacipran: AE, adverse drug reaction
milnacipran: DV, drug development
milnacipran: DT, drug therapy
milnacipran: PD, pharmacology
venlafaxine: AE, adverse drug reaction
venlafaxine: DV, drug development
venlafaxine: DT, drug therapy
venlafaxine: PD, pharmacology
duloxetine: AE, adverse drug reaction
duloxetine: DV, drug development
duloxetine: DT, drug therapy
duloxetine: PD, pharmacology
cannabis derivative: AE, adverse drug reaction
cannabis derivative: DV, drug development
cannabis derivative: DT, drug therapy
cannabis derivative: PD, pharmacology
unindexed drug

CAS REGISTRY NO.: (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (parecoxib) 198470-84-7, 198470-85-8; (valdecoxib) 181695-72-7; (etoricoxib) 202409-33-4, 202409-40-3; (licofelone) 156897-06-2; (lumiracoxib) 220991-20-8; (zileuton) 111406-87-2, 132880-11-6; (lamotrigine) 84057-84-1; (oxcarbazepine) 28721-07-5; (tetrodotoxin) 4368-28-9, 4664-41-9; (topiramate) 97240-79-4; (pregabalin) 148553-50-8; (dextromethorphan) 125-69-9, 125-71-3; (morphine) 52-26-6, 57-27-2; (memantine) 19982-08-2, 41100-52-1; (decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3 isoquinolinecarboxylic acid) 154652-83-2; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (venlafaxine) 93413-69-5; (duloxetine) 116539-59-4, 136434-34-9; (cannabis derivative) 38458-58-1

CHEMICAL NAME: Ml 3000; Cox 189; Ly 293558

L42 ANSWER 41 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003305324 EMBASE

TITLE: Efficacy of milnacipran for glossodynia patients.

AUTHOR: Toyofuku A.
CORPORATE SOURCE: A. Toyofuku, Dept. of Dentistry and Oral Surgery, School of Medicine, Fukuoka University, 7-45-1 Nanakuma, Johnan-ku, Fukuoka, Japan. toyofuku@minf.med.fukuoka-u.ac.jp
SOURCE: International Journal of Psychiatry in Clinical Practice, (2003) 7/SUPPL. 1 (23-24).
Refs: 6
ISSN: 1365-1501 CODEN: IJPCFZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Pain and depression are thought to arise from a common neurochemical dysfunction at the level of noradrenergic and serotonergic neurons, and antidepressants are used to treat chronic pain. The dual action tricyclic antidepressants are more potent in relieving pain than the selective serotonin reuptake inhibitors. Glossodynia is chronic pain and burning sensation in the tongue often associated with depression. Patients suffering from glossodynia were treated with the serotonin and noradrenaline reuptake inhibitor, milnacipran, which has been recently launched in Japan. Milnacipran was found to be effective in the relief of the chronic glossodynia and well tolerated.

CONTROLLED TERM: Medical Descriptors:
*glossodynia: DT, drug therapy
chronic pain: DT, drug therapy
treatment outcome
rating scale
drug effect
visual analog scale
constipation: SI, side effect
heart palpitation: SI, side effect
human
male
female
clinical article
adult
conference paper
priority journal
Drug Descriptors:
*milnacipran: AE, adverse drug reaction
*milnacipran: DT, drug therapy
*milnacipran: PD, pharmacology
antidepressant agent: DT, drug therapy
serotonin uptake inhibitor: DT, drug therapy
serotonin uptake inhibitor: PD, pharmacology
noradrenalin uptake inhibitor: DT, drug therapy
noradrenalin uptake inhibitor: PD, pharmacology
CAS REGISTRY NO.: (milnacipran) **101152-94-7, 86181-08-0, 92623-85-3**

L42 ANSWER 42 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003399422 EMBASE
TITLE: [Substance P-antagonism in treatment of major depressive disorder: An antidepressant strategy for the future?]. SUBSTANZ-P-ANTAGONISMUS ZUR BEHANDLUNG VON DEPRESSION: EIN WIRKPRINZIP FUR DIE ZUKUNFT?.
AUTHOR: Wiesegger G.; Tauscher J.; Kasper S.

CORPORATE SOURCE: Dr. G. Wiesegger, Universitatsklinik fur Psychiat., Klin. Abt. fur Allg. Psychiat., AKH Wien, Wahringer Gurtel 18-20, A-1090 Wien, Austria. Georg.Wiesegger@akh-wien.ac.at
SOURCE: Journal fur Neurologie, Neurochirurgie und Psychiatrie, (2003) 4/3 (21-23).
Refs: 14
ISSN: 1608-1587 CODEN: JNNPBV
COUNTRY: Austria
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ABSTRACT:
Neurokinins (NK, Tachykinins, Neuropeptides) are co-transmitters of neuronal monoaminergic transmission. Up to date, three NK-receptors have been found in humans. Animal models showed antidepressant effects when the NK1-receptor was antagonized. MK-0869 (generic name: Aprepitant) is a potent highly selective antagonist of Substance P at the central NK1-receptor. MK-0869/aprepitant was shown to exhibit efficacy compared to paroxetine in treatment of depression with better tolerability due to less gastrointestinal side effects. Besides a lack of direct cardiovascular effects, a lower incidence of sexual dysfunction compared to traditional antidepressants can be expected. Placebo-controlled studies have to be conducted to investigate this topic. Efficacy of MK-0869/aprepitant is also investigated in herpes-neuralgia and chemotherapy-induced emesis, and above that other NK1-antagonists in migraine und asthma bronchiale. More investigations are needed to show the efficacy of this new pharmacological principle in the treatment of depression. From recent data a promising profile of effects and side effects can be concluded. Due to problems of SSRIs in patients with affective disorders concerning tolerability and compliance this might be an important step in development of modern antidepressants.

CONTROLLED TERM: Medical Descriptors:
*major depression: DT, drug therapy
monoaminergic system
animal model
drug efficacy
depression: DT, drug therapy
drug tolerability
gastrointestinal symptom: SI, side effect
sexual dysfunction: SI, side effect
postherpetic neuralgia: DT, drug therapy
chemotherapy induced emesis: DT, drug therapy
migraine: DT, drug therapy
asthma: DT, drug therapy
mood disorder: DT, drug therapy
patient compliance
somnolence: SI, side effect
nausea: SI, side effect
human
clinical trial
review
Drug Descriptors:
*substance P antagonist: DT, drug therapy
neurokinin
tachykinin
neuropeptide
tachykinin receptor
neurokinin 1 receptor

substance P
2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine: AE, adverse drug reaction
2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine: CT, clinical trial
2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine: CM, drug comparison
2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine: DT, drug therapy
2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine: PD, pharmacology
antidepressant agent: CM, drug comparison
antidepressant agent: DT, drug therapy
serotonin uptake inhibitor: CM, drug comparison
serotonin uptake inhibitor: DT, drug therapy
paroxetine: CM, drug comparison
paroxetine: DT, drug therapy
citalopram: DT, drug therapy
escitalopram: DT, drug therapy
fluoxetine: DT, drug therapy
fluvoxamine: DT, drug therapy
sertraline: DT, drug therapy
milnacipran: DT, drug therapy
venlafaxine: DT, drug therapy
neuropeptide Y
enkephalin
1 [2 [3 (3,4 dichlorophenyl) 1 (3 isopropoxyphenylacetyl) 3 piperidyl]ethyl] 4 phenyl 1 azoniabicyclo[2.2.2]octane chloride: DT, drug therapy
n benzyl n2 [4 hydroxy 1 [(1 methyl 1h indol 3 yl)carbonyl]prolyl] n methyl 3 (2 naphthyl)alaninamide: DT, drug therapy
nkp 608: DT, drug therapy
cgp 60829: DT, drug therapy
unclassified drug
aprepitant
fluvoxamine maleate
dalcopram
efectin

CAS REGISTRY NO.: (substance P) 33507-63-0; (2 [1 [3,5 bis(trifluoromethyl)phenyl]ethoxy] 3 (4 fluorophenyl) 4 (3 oxo 1,2,4 triazol 5 ylmethyl)morpholine) 170729-80-3, 221350-96-5; (paroxetine) 61869-08-7; (citalopram) 59729-33-8; (escitalopram) 128196-01-0, 219861-08-2; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine) 54739-18-3; (sertraline) 79617-96-2; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (venlafaxine) 93413-69-5; (neuropeptide Y) 82785-45-3, 83589-17-7; (1 [2 [3 (3,4 dichlorophenyl) 1 (3 isopropoxyphenylacetyl) 3 piperidyl]ethyl] 4 phenyl 1 azoniabicyclo[2.2.2]octane chloride) 153050-21-6, 154728-59-3; (n benzyl n2 [4 hydroxy 1 [(1 methyl 1h indol 3 yl)carbonyl]prolyl] n methyl 3 (2 naphthyl)alaninamide) 138449-07-7; (fluvoxamine maleate) 61718-82-9

CHEMICAL NAME: Cgp 60829; Nkp 608; Fk 888; Sr 140333; L 754030; Mk 0869; Efectin; Dalcopram; Ixel; Tresleen; Gladem; Seroxat; Floxyfral; Fluctine; Cipralex; Seropram; Aprepitant

L42 ANSWER 43 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003305321 EMBASE
TITLE: Evidence-based prescribing of antidepressants.
AUTHOR: Montgomery S.A.
CORPORATE SOURCE: S.A. Montgomery, PO Box 8751, London W13 8WH, United Kingdom. stuart@samontgomery.co.uk
SOURCE: International Journal of Psychiatry in Clinical Practice, (2003) 7/SUPPL. 1 (9-14).
Refs: 38
ISSN: 1365-1501 CODEN: IJPCFZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Modern antidepressants are required to undergo extensive clinical investigation before their commercialisation is authorised, and this provides the basis for the "evidence-based recommendations" for their use. Because of the rigorous methodology required in formal clinical trials in order to establish efficacy, the population studied and the conditions of use of a treatment are likely to differ substantially from those encountered in everyday clinical practice. There is limited opportunity in clinical trials for casual observation of the effects of the drug, its efficacy in patients with co-morbid disorders, or its use outside of the strict indication for which the compound seeks a licence. The observations, case studies, open trials and small comparative trials that are conducted on an antidepressant after it has been launched can provide important information. The less rigorous methodology is to some extent compensated by their relevance to everyday prescribing and their openness to chance discoveries. They can provide complementary information on responder characteristics and acceptance of side effects and can suggest potential conditions and indications not originally foreseen. This body of data can be referred to as "prescribing-based evidence". The obvious complementarity of these two bodies of information is illustrated by reference to the serotonin and noradrenaline reuptake inhibitor (SNRI), milnacipran, which has been the subject of intense post-marketing study, especially in Japan. The newly discovered efficacy of milnacipran in chronic pain, both associated with depression and in conditions such as fibromyalgia, is an example of the extended understanding that can be obtained by such studies.

CONTROLLED TERM: Medical Descriptors:
*evidence based medicine
*prescription
*depression: CO, complication
*depression: DI, diagnosis
*depression: DT, drug therapy
drug effect
drug efficacy
drug indication
methodology
postmarketing surveillance
chronic pain: DT, drug therapy
fibromyalgia: DT, drug therapy
practice guideline
bipolar disorder: DT, drug therapy
schizophrenia: DT, drug therapy
bulimia: DT, drug therapy
clinical feature

human
conference paper
priority journal
Drug Descriptors:
*antidepressant agent: DT, drug therapy
serotonin uptake inhibitor: DT, drug therapy
noradrenalin uptake inhibitor: DT, drug therapy
milnacipran: DT, drug therapy
tricyclic antidepressant agent: DT, drug therapy
imipramine: DT, drug therapy
CAS REGISTRY NO.: (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**; (imipramine) 113-52-0, 50-49-7

L42 ANSWER 44 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002357309 EMBASE
TITLE: Treatment of fibromyalgia with sibutramine hydrochloride monohydrate: Comment on the article by Goldenberg et al [6] (multiple letters).
AUTHOR: Palangio M.; Flores J.A.; Joyal S.V.; Goldenberg D.; Sandhu T.
CORPORATE SOURCE: M. Palangio, Abbott Laboratories, Parsippany, NJ, United States
SOURCE: Arthritis and Rheumatism, (1 Sep 2002) 46/9 (2545-2546). ISSN: 0004-3591 CODEN: ARHEAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
***fibromyalgia: DT, drug therapy**
clinical feature
disease course
treatment outcome
visual analog scale
pain: CO, complication
pain: DT, drug therapy
pain: ET, etiology
disease severity
drug withdrawal
retrospective study
physical capacity
drug tolerability
serotonin syndrome: SI, side effect
autonomic dysfunction: SI, side effect
sedation
side effect: SI, side effect
fatigue: SI, side effect
orthostatic hypotension: SI, side effect
anticholinergic effect
human
male
female
major clinical study
clinical trial
controlled study
aged
adult
letter

priority journal
Drug Descriptors:
*sibutramine: AE, adverse drug reaction
*sibutramine: CT, clinical trial
*sibutramine: DT, drug therapy
prednisone: DT, drug therapy
buspirone: DT, drug therapy
zolpidem: DT, drug therapy
fentanyl: DT, drug therapy
fentanyl: TD, transdermal drug administration
hydrocodone: CB, drug combination
hydrocodone: DT, drug therapy
hydrocodone: PO, oral drug administration
paracetamol: CB, drug combination
paracetamol: DT, drug therapy
amitriptyline: DT, drug therapy
fluoxetine: DT, drug therapy
venlafaxine: DT, drug therapy
duloxetine: DT, drug therapy
milnacipran: DT, drug therapy
CAS REGISTRY NO.: (sibutramine) 106650-56-0; (prednisone) 53-03-2; (buspirone) 33386-08-2, 36505-84-7; (zolpidem) 82626-48-0; (fentanyl) 437-38-7; (hydrocodone) 125-29-1, 25968-91-6, 34366-67-1; (paracetamol) 103-90-2; (amitriptyline) 50-48-6, 549-18-8; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (venlafaxine) 93413-69-5; (duloxetine) 116539-59-4, 136434-34-9; (milnacipran) **101152-94-7**, **86181-08-0**, **92623-85-3**

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:42:27 ON 29 SEP 2004
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DICTIONARY FILE UPDATES: 28 SEP 2004 HIGHEST RN 753424-73-6

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http://www.cas.org/ONLINE/DBSS/registryss.html

=> s 101152-94-7 or 86181-08-0 or 92623-85-3

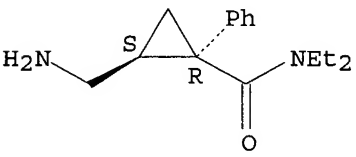
1 101152-94-7
(101152-94-7/RN)
1 86181-08-0
(86181-08-0/RN)
1 92623-85-3
(92623-85-3/RN)

L43 2 101152-94-7 OR 86181-08-0 OR 92623-85-3

=> d ide l43 1-2

L43 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **101152-94-7** REGISTRY
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, monohydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, monohydrochloride, cis-(.+-.)-
OTHER NAMES:
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, monohydrochloride, cis-
CN Dalcipran
CN F 2207
CN Ixel
CN Milnacipran hydrochloride
FS STEREOSEARCH
DR **86181-08-0**
MF C15 H22 N2 O . Cl H
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
CRN (92623-85-3)

Relative stereochemistry.



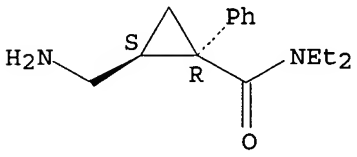
● HCl

23 REFERENCES IN FILE CA (1907 TO DATE)
23 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **92623-85-3** REGISTRY
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, cis-(.+-.)-
OTHER NAMES:
CN (.+-.)-Milnacipran
CN (1R,2S)-rel-2-(Aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide

CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, cis-
CN Midalcipran
CN Milnacipran
CN Toledomin
FS STEREOSEARCH
DR 105310-09-6
MF C15 H22 N2 O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

194 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
198 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> fil medl; d que l51
FILE 'MEDLINE' ENTERED AT 14:51:31 ON 29 SEP 2004

 FILE LAST UPDATED: 28 SEP 2004 (20040928/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L28      170781 SEA FILE=MEDLINE ABB=ON  PAIN+NT/CT
L29        2830 SEA FILE=MEDLINE ABB=ON  FIBROMYALGIA/CT
L30        2518 SEA FILE=MEDLINE ABB=ON  FATIGUE SYNDROME, CHRONIC/CT
L50         642 SEA FILE=MEDLINE ABB=ON  (SEROTONIN(5A)(NOREPINEPHRINE OR
                NORADRENALINE)(5A)?UPTAKE?(5A)INHIBIT?)
L51          39 SEA FILE=MEDLINE ABB=ON  L50 AND (L28 OR L29 OR L30)


=> s l51 not l31
L57          36 L51 NOT L31

=> d iall l57 1-36; fil hom

L57  ANSWER 1 OF 36     MEDLINE on STN
ACCESSION NUMBER:   2004347516     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15250433
TITLE:              Venlafaxine in the treatment of atypical facial pain: a
                    randomized controlled trial.
AUTHOR:             Forssell Heli; Tasmuth Tiina; Tenovuo Olli; Hampf Goran;
                    Kalso Eija
CORPORATE SOURCE:   Department of Oral Diseases/Pain Clinic, Turku University
                    Central Hospital Turku, Finland.. heli.forssell@tyks.fi
SOURCE:             Journal of orofacial pain, (2004 Spring) 18 (2) 131-7.
                    Journal code: 9418507. ISSN: 1064-6655.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (CLINICAL TRIAL)
                    Journal; Article; (JOURNAL ARTICLE)
                    (MULTICENTER STUDY)
                    (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE:           English
FILE SEGMENT:       Dental Journals
ENTRY MONTH:        200408
ENTRY DATE:         Entered STN: 20040715
                    Last Updated on STN: 20040810
                    Entered Medline: 20040809
ABSTRACT:
AIMS: To study in a randomized placebo-controlled design the efficacy of the
antidepressant venlafaxine, a serotonin and a weak
***noradrenaline***   reuptake inhibitor, in the treatment
of atypical facial pain (AFP). METHODS: The study was a randomized,
double-blind, crossover comparison of venlafaxine and a placebo. It consisted
of 2 treatment periods, each of 4 weeks' duration, separated by a 2-week
washout period. Thirty patients suffering from chronic pain who had been
diagnosed with AFP after a thorough clinical examination were recruited. Pain
```

intensity and pain relief were registered at 6 visits. Anxiety, depression, and adverse effects were recorded. Venous blood samples were collected at the end of each treatment period for the determination of serum levels of venlafaxine and its metabolites. RESULTS: Twenty patients completed the trial. Eight patients discontinued because of adverse effects and 2 patients were excluded because of noncompliance. Two patients completed the trial but were excluded from the analysis because they experienced no pain at the baseline visit. There was no significant difference in pain intensity reduction between the maximum tolerated dose of venlafaxine (75 mg in most cases) and the placebo. Pain relief was significantly greater with venlafaxine than with the placebo treatment. Significantly more escape medication was consumed during the placebo period compared with the venlafaxine period. No significant correlation was found between the serum concentration of the drug and the response to treatment. Anxiety and depression scores did not differ between venlafaxine and placebo treatment. Adverse effects were equally common during both treatments. CONCLUSION: Venlafaxine was only modestly effective in the treatment of AFP.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Analgesics: BL, blood
*Analgesics: TU, therapeutic use
Cross-Over Studies
Cyclohexanols: BL, blood
*Cyclohexanols: TU, therapeutic use
Double-Blind Method
***Facial Pain: DT, drug therapy**
Middle Aged
Pain Measurement
Serotonin Uptake Inhibitors: BL, blood
*Serotonin Uptake Inhibitors: TU, therapeutic use
Statistics, Nonparametric
Treatment Outcome

CAS REGISTRY NO.: 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Analgesics); 0 (Cyclohexanols); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 2 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2004264085 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15162896

TITLE: Treatment of pain syndromes with venlafaxine.

AUTHOR: Grothe Dale R; Scheckner Brian; Albano Dominick

CORPORATE SOURCE: Global Medical Communications, Neuroscience, Wyeth Pharmaceuticals, Collegeville, Pennsylvania 19426, USA.

SOURCE: Pharmacotherapy, (2004 May) 24 (5) 621-9. Ref: 59
Journal code: 8111305. ISSN: 0277-0008.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200408

ENTRY DATE: Entered STN: 20040528
Last Updated on STN: 20040818
Entered Medline: 20040817

ABSTRACT:

Major depressive disorder (MDD) and anxiety disorders such as generalized anxiety disorder (GAD) are often accompanied by chronic painful symptoms. Examples of such symptoms are backache, headache, gastrointestinal pain, and joint pain. In addition, pain generally not associated with major depression or an anxiety disorder, such as peripheral neuropathic pain (e.g., diabetic

neuropathy and postherpetic neuralgia), cancer pain, and fibromyalgia, can be challenging for primary care providers to treat. Antidepressants that block reuptake of both serotonin and norepinephrine, such as the tricyclic antidepressants (e.g., amitriptyline), have been used to treat pain syndromes in patients with or without comorbid MDD or GAD. Venlafaxine, a ***serotonin*** and **norepinephrine reuptake** ***inhibitor*** , has been safe and effective in animal models, healthy human volunteers, and patients for treatment of various pain syndromes. The use of venlafaxine for treatment of pain associated with MDD or GAD, neuropathic pain, headache, fibromyalgia, and postmastectomy pain syndrome is reviewed. Currently, no antidepressants, including venlafaxine, are approved for the treatment of chronic pain syndromes. Additional randomized, controlled trials are necessary to fully elucidate the role of venlafaxine in the treatment of chronic pain.

CONTROLLED TERM: Check Tags: Human
Analgesics: AE, adverse effects
*Analgesics: TU, therapeutic use
Animals
*Anxiety Disorders: CO, complications
Anxiety Disorders: PP, physiopathology
Cyclohexanols: AE, adverse effects
*Cyclohexanols: TU, therapeutic use
*Depression, Involutional: CO, complications
Depression, Involutional: PP, physiopathology
***Pain**
Pain: DT, drug therapy
Pain: ET, etiology
Pain: PP, physiopathology
Pain, Postoperative: DT, drug therapy
Randomized Controlled Trials

CAS REGISTRY NO.: 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Analgesics); 0 (Cyclohexanols)

L57 ANSWER 3 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2004125192 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15017493

TITLE: Effects of venlafaxine, buspirone, and placebo on colonic sensorimotor functions in healthy humans.

AUTHOR: Chial Heather J; Camilleri Michael; Ferber Irene; Delgado-Aros Silvia; Burton Duane; McKinzie Sanna; Zinsmeister Alan R

CORPORATE SOURCE: Clinical Enteric Neuroscience Translational and Epidemiological Research (C.E.N.T.E.R.) Program, Mayo Clinic, Rochester, Minnesota 55905, USA.

CONTRACT NUMBER: K24-DK02638 (NIDDK)
R01-DK54681 (NIDDK)
RR00585 (NCRR)

SOURCE: Clin Gastroenterol Hepatol, (2003 May) 1 (3) 211-8.
Journal code: 101160775. ISSN: 1542-3565.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200404

ENTRY DATE: Entered STN: 20040313
Last Updated on STN: 20040402
Entered Medline: 20040401

ABSTRACT:

BACKGROUND & AIMS: We have shown that venlafaxine-XR, a **serotonin** (5-HT) and **norepinephrine reuptake inhibitor**,

enhanced gastric accommodation, whereas buspirone, a 5-HT(1A) receptor agonist, reduced postprandial symptoms after a fully satiating meal. Our aim was to compare the effects of venlafaxine, buspirone, and placebo on colonic sensorimotor functions in healthy adults. METHODS: In this randomized, double-blind, parallel-group, placebo-controlled trial of 60 healthy adults, we assessed the effects of oral venlafaxine, 150 mg; buspirone, 20 mg; and placebo on colonic sensorimotor functions. RESULTS: Venlafaxine increased colonic compliance relative to placebo; thus it decreased the intracolonic balloon pressure at half-maximum volume (P = 0.001) and altered the overall shape of the compliance curve, beta (P = 0.01). Venlafaxine also decreased fasting colonic tone (P = 0.02) and the tonic response to a meal (P = 0.003) compared with placebo; no differences in high amplitude phasic contractile events were observed. Pressure thresholds for first sensation (P = 0.1) and gas (P = 0.07) were not statistically significant with venlafaxine. The increase in pain scores per unit pressure during phasic distentions were affected by treatment (P = 0.02), with smallest changes on venlafaxine and highest on placebo. Buspirone did not significantly alter colonic compliance, tone, or sensation relative to placebo. CONCLUSIONS: Venlafaxine alters colonic compliance and tone, and tends to reduce sensation during colonic distention in healthy humans. These data support the need for further clinical and physiologic studies of venlafaxine in colonic disorders affecting motor and possibly sensory functions.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
*Anti-Anxiety Agents: PD, pharmacology
*Antidepressive Agents, Second-Generation: PD, pharmacology
*Buspirone: PD, pharmacology
Colon: DE, drug effects
Colon: IR, innervation
*Colon: PH, physiology
Compliance
*Cyclohexanols: PD, pharmacology
Double-Blind Method
Fasting
Pain
Postprandial Period
Pressure
Reference Values
Sensory Thresholds
*Serotonin Agonists: PD, pharmacology
*Serotonin Uptake Inhibitors: PD, pharmacology

CAS REGISTRY NO.: 36505-84-7 (Buspirone); 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Anti-Anxiety Agents); 0 (Antidepressive Agents, Second-Generation); 0 (Cyclohexanols); 0 (Serotonin Agonists); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 4 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2004081981 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14971531

TITLE: Two doses of oral sustained-release tramadol do not reduce pain or morphine consumption after modified radical mastectomy: a randomized, double blind, placebo-controlled trial.

AUTHOR: Thienthong Somboon; Krisanaprakornkit Wimonrat; Taesiri Worranut; Thaninsurat Nuanchan; Utsahapanich Siriporn; Klaichanad Chongsuk

CORPORATE SOURCE: Department of Anesthesiology, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

SOURCE: Journal of the Medical Association of Thailand = Chotmaihet thangphaet, (2004 Jan) 87 (1) 24-32.

Journal code: 7507216. ISSN: 0125-2208.
PUB. COUNTRY: Thailand
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040220
Last Updated on STN: 20040313
Entered Medline: 20040312

ABSTRACT:
BACKGROUND: Tramadol is a weak opioid agonist with antinociceptive effects through its action on the mu-receptor and by **inhibiting** the neuronal re- **uptake** of both **noradrenaline** and **serotonin**.
Tramadol is commonly used for treatment of mild to moderate post-operative pain. An oral form of sustained-release tramadol (SR) was recently formulated for reducing the administration frequency from qid to bid. OBJECTIVE: To evaluate the analgesic efficacy and safety of two doses of oral tramadol SR for the treatment of pain after modified radical mastectomy. STUDY DESIGN: Randomized, double blind, placebo-controlled trial. METHOD: Fifty women were randomly allocated to receive either tramadol SR 100 mg (group T), or placebo tablet (group P) orally approximately 1 hour before surgery with a repeat dose administered 12 hours later by nurses not apprised of the patient groupings. All patients received the standard general anesthesia. Post-operatively, nurses in the research team assessed pain using a visual analog scale 0-100 mm at rest (rVAS) and during arm movements (mVAS) at admission to postanesthesia care unit (PACU) (T0) and 2 (T2), 6 (T6), 12 (T12) and 24 (T24) hours after surgery. Rescue analgesia was provided for 24 hours via a morphine-loaded patient-controlled analgesia (PCA) device at 1 mg bolus with a 5-minute lockout interval. Cumulative morphine consumption and adverse events were recorded. RESULTS: Twenty-five patients with comparable baseline characteristics from each group were studied. The proportions of patients with VAS > 30 (both rVAS and mVAS) at each measurement period were not significantly different between the groups except for the mVAS at T24, where the proportion in group T was higher than group P (48% vs 20%, 95% CI of difference: -53%, -3%, p = 0.04). The median morphine consumption in both groups at T2, T6, T12 and T24 were comparable. No serious adverse effects were observed; however, patients in group T reported nausea and vomiting more than group P (56% vs 24%, p = 0.02). CONCLUSION: Two doses of oral tramadol SR 100 mg had no effect on post-operative pain scores and morphine consumption in patients who underwent modified radical mastectomy. In fact, more patients in the tramadol group reported nausea and vomiting than the placebo group.

CONTROLLED TERM: Check Tags: Female; Human; Support, Non-U.S. Gov't
Administration, Oral
Adolescent
Adult
*Analgesics, Opioid: AD, administration & dosage
Breast Neoplasms: SU, surgery
Double-Blind Method
*Mastectomy, Modified Radical: AE, adverse effects
Middle Aged
*Morphine: AD, administration & dosage
***Pain, Postoperative: DT, drug therapy**
*Tramadol: AD, administration & dosage
Treatment Outcome
CAS REGISTRY NO.: 27203-92-5 (Tramadol); 57-27-2 (Morphine)
CHEMICAL NAME: 0 (Analgesics, Opioid)

L57 ANSWER 5 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2004013101 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14709757

TITLE: Effects of duloxetine on painful physical symptoms associated with depression.
AUTHOR: Goldstein David J; Lu Yili; Detke Michael J; Hudson James; Iyengar Smriti; Demitrack Mark A
CORPORATE SOURCE: Department of Psychitry adn the Department of Pharmacology adn toxicology, Indiana Unibersity School of Medicine, Indianapolis, USA.. DJGoldstein@consultPRNC.com
SOURCE: Psychosomatics, (2004 Jan-Feb) 45 (1) 17-28.
Journal code: 0376506. ISSN: 0033-3182.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040108
Last Updated on STN: 20040213
Entered Medline: 20040212

ABSTRACT:
Painful physical symptoms are common features of major depressive disorder and may be the presenting complaints in primary care settings. The effect of the dual **serotonin** (5-HT) and **norepinephrine reuptake** ***inhibitor*** duloxetine on emotional and painful physical symptoms in outpatients with major depressive disorder was evaluated in three randomized, double-blind, placebo-controlled trials. The trials' primary objective was to evaluate the effect of duloxetine on mood, and subjects were not enrolled on the basis of presence, type, or severity of pain. However, the pain-relieving effects of duloxetine were evaluated by a priori defined analyses of results from a visual analogue scale and the Somatic Symptom Inventory. Compared with placebo, duloxetine was associated with significant reduction in pain severity. The authors concluded that duloxetine reduces the painful physical symptoms of depression.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Adult
*Antidepressive Agents: TU, therapeutic use
*Depressive Disorder: DT, drug therapy
Depressive Disorder: PP, physiopathology
Depressive Disorder: PX, psychology
Dose-Response Relationship, Drug
Double-Blind Method
Norepinephrine: ME, metabolism
***Pain: DT, drug therapy**
Pain: PP, physiopathology
Pain Measurement
Serotonin: ME, metabolism
*Serotonin Uptake Inhibitors: TU, therapeutic use
*Thiophenes: TU, therapeutic use
Treatment Outcome
CAS REGISTRY NO.: 116539-58-3 (duloxetine); 50-67-9 (Serotonin); 51-41-2 (Norepinephrine)
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents); 0 (Serotonin Uptake Inhibitors); 0 (Thiophenes)

L57 ANSWER 6 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003600863 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14682027
TITLE: Physical symptoms comorbid with depression and the new antidepressant duloxetine.
AUTHOR: Bailey Katharine P

CORPORATE SOURCE: Yale University School of Nursing, New Haven, Connecticut, USA.. katharine.bailey@yale.edu
SOURCE: Journal of psychosocial nursing and mental health services, (2003 Dec) 41 (12) 13-8. Ref: 33
Journal code: 8200911. ISSN: 0279-3695.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Nursing Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031220
Last Updated on STN: 20040117
Entered Medline: 20040116

ABSTRACT:
Most general descriptions of depression that date back to Hippocrates, including the DSM-IV, have listed gastrointestinal problems, sleep disturbances, headaches, appetite changes, and aches and pains of a diffuse nature as common features of the disorder. In addition, physical symptoms have a strong association with psychiatric disorders, and the presence of any physical symptom may increase the likelihood of a mood or anxiety disorder by two-fold or three-fold. A growing body of evidence suggests that serotonin and norepinephrine may share neurochemical mechanisms that tie depression and physical symptoms together. Both selective serotonin reuptake inhibitors alone and antidepressant agents that incorporate both **serotonin** and ***norepinephrine*** **reuptake inhibition** have shown evidence of relieving physical symptoms. Given the additional disease burden caused by physical symptoms in depression, it is vital that antidepressant agents that effectively treat the physical symptoms and chronic pain associated with depression be used.

CONTROLLED TERM: Check Tags: Human
Adrenergic Uptake Inhibitors: PD, pharmacology
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Antidepressive Agents: PD, pharmacology
*Antidepressive Agents: TU, therapeutic use
Anxiety Disorders
Comorbidity
*Depressive Disorder: CO, complications
Depressive Disorder: DI, diagnosis
*Depressive Disorder: DT, drug therapy
Depressive Disorder: PP, physiopathology
*Gastrointestinal Diseases: ET, etiology
Gastrointestinal Diseases: PC, prevention & control
Mood Disorders
Norepinephrine: PH, physiology
***Pain: ET, etiology**
Pain: PC, prevention & control
Psychophysiologic Disorders
Serotonin: PH, physiology
Serotonin Uptake Inhibitors: PD, pharmacology
*Serotonin Uptake Inhibitors: TU, therapeutic use
*Sleep Disorders: ET, etiology
Sleep Disorders: PC, prevention & control
Thiophenes: PD, pharmacology
*Thiophenes: TU, therapeutic use
Treatment Outcome
CAS REGISTRY NO.: 116539-58-3 (duloxetine); 50-67-9 (Serotonin); 51-41-2 (Norepinephrine)
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents); 0 (Serotonin Uptake Inhibitors); 0 (Thiophenes)

L57 ANSWER 7 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003563146 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14650359
TITLE: Tramadol--the impact of its pharmacokinetic and pharmacodynamic properties on the clinical management of pain.
AUTHOR: Klotz Ulrich
CORPORATE SOURCE: Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany.. ulrich.klotz@ikp-stuttgart.de
SOURCE: Arzneimittel-Forschung, (2003) 53 (10) 681-7. Ref: 35
Journal code: 0372660. ISSN: 0004-4172.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20031224
Entered Medline: 20031223

ABSTRACT:
Tramadol (CAS 36282-47-0) plays an important role in the management of pain. With its dual mechanism of action (opioid agonist; weak **noradrenaline** and **serotonin reuptake inhibitor**) tramadol provides a kind of combined/adjuvant pain therapy. Besides its proven clinical efficacy tramadol is a safe drug as respiratory depression, cardiovascular side effects, drug abuse and dependence are of minor clinical relevance, unlike some other opioids. Following oral administration the bioavailability of tramadol is high (70-90%) and with new slow release preparations twice daily administration enables effective pain control. Tramadol is characterised by low plasma protein binding (20%) and quite extensive tissue distribution (apparent volume of distribution about 3 l/kg). Elimination is primarily by the hepatic route (metabolism by CYP2D6 to an active metabolite and by CYP3A4 and CYP2B6) and partly by the renal route (up to 30% of dose). Elimination half-lives of the active agents range between 4.5 and 9.5 h and total plasma clearance of tramadol is moderately high (600 ml/min). The interaction potential of tramadol is neglectable, as it does not affect the disposition of other drugs. It should be taken into account that inducers (e.g. carbamazepine) or inhibitors (e.g. quinidine for CY2D6) of drug metabolism might modify the elimination of tramadol. Likewise, if kidney (creatinine clearance below 30 ml/min) or hepatic function is severely impaired, some dosage reduction (approximately by 50%) or extension of the dosage interval should be considered. In conclusion, tramadol is an effective and safe analgesic with a very low interaction potential. Therefore it represents a drug of first choice if moderate to severe pain states have to be treated in pediatric, adult and elderly patients including those with poor cardiopulmonary function.

CONTROLLED TERM: Check Tags: Human
Analgesics, Opioid: AD, administration & dosage
Analgesics, Opioid: AE, adverse effects
*Analgesics, Opioid: PK, pharmacokinetics
*Analgesics, Opioid: TU, therapeutic use
Drug Interactions
***Pain: DT, drug therapy**
Tramadol: AD, administration & dosage
Tramadol: AE, adverse effects
*Tramadol: PK, pharmacokinetics
*Tramadol: TU, therapeutic use
CAS REGISTRY NO.: 27203-92-5 (Tramadol)
CHEMICAL NAME: 0 (Analgesics, Opioid)

L57 ANSWER 8 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003488516 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14565792
TITLE: Venlafaxine treatment of fibromyalgia.
AUTHOR: Sayar Kemal; Aksu Gokhan; Ak Ismail; Tosun Mehmet
CORPORATE SOURCE: Karadeniz Technical University School of Medicine, Farabi Hospital, Trabzon, Turkey.. mkemalsayar@superonline.com
SOURCE: Annals of pharmacotherapy, (2003 Nov) 37 (11) 1561-5. Journal code: 9203131. ISSN: 1060-0280.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20031021
Last Updated on STN: 20040306
Entered Medline: 20040305

ABSTRACT:
BACKGROUND: Although the pathophysiology of fibromyalgia is unknown, central monoaminergic transmission may play a role. Antidepressants have proved to be successful in alleviating symptoms of fibromyalgia. Medications that act on multiple neurotransmitters may be more effective in symptom management. OBJECTIVE: To assess the efficacy of venlafaxine, a potent **inhibitor** of both **norepinephrine** and **serotonin reuptake**, in the treatment of patients with fibromyalgia. METHODS: Fifteen patients with fibromyalgia were assessed prior to and after treatment with fixed-dose venlafaxine 75 mg/d. Before initiation of pharmacotherapy, patients were interviewed with the Structured Clinical Interview for Axis I disorders in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition. The study lasted for 12 weeks, and patients were evaluated in weeks 6 and 12. The primary outcome measures were the Fibromyalgia Impact Questionnaire (FIQ) total score and pain score. The anxiety and depression levels of the patients were measured with the Beck Depression, the Beck Anxiety, the Hamilton Anxiety, and the Hamilton Depression scales. RESULTS: There was a significant improvement in the mean intensity of pain (F = 14.3; p = 0.0001) and in the disability caused by fibromyalgia (F = 42.7; p = 0.0001) from baseline to week 12 of treatment. The depression and anxiety scores also decreased significantly from baseline to week 12. The improvement in the FIQ scores did not correlate with the decrease of scores in both patient- and physician-rated depression and anxiety inventories. Change in pain scores also was not correlated with the change in depression and anxiety scores. CONCLUSIONS: Venlafaxine was quite promising in alleviating the pain and disability associated with fibromyalgia. This effect seems to be independent of its anxiolytic and antidepressant properties. Blockade of both norepinephrine and serotonin reuptake might be more effective than blockade of either neurotransmitter alone in the treatment of fibromyalgia.

CONTROLLED TERM: Check Tags: Female; Human
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Adult
Anxiety: CO, complications
Anxiety: DT, drug therapy
*Cyclohexanols: TU, therapeutic use
Depression: CO, complications
Depression: DT, drug therapy
Fibromyalgia: CO, complications
***Fibromyalgia: DT, drug therapy**
Pain: DT, drug therapy
Pain: ET, etiology
*Serotonin Uptake Inhibitors: TU, therapeutic use
CAS REGISTRY NO.: 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Cyclohexanols); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 9 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003477724 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14552654
TITLE: Efficacy and tolerability of duloxetine, a novel dual reuptake inhibitor, in the treatment of major depressive disorder.
AUTHOR: Schatzberg Alan F
CORPORATE SOURCE: Department of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305-5717, USA..
afschatz@stanford.edu
SOURCE: Journal of clinical psychiatry, (2003) 64 Suppl 13 30-7.
Ref: 45
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20031015
Last Updated on STN: 20040121
Entered Medline: 20040120

ABSTRACT:
Although highly selective antidepressants such as the selective serotonin reuptake inhibitors represent an advance over older drugs with respect to tolerability, they are not more effective than previous agents. Antidepressants that enhance transmission in more than one monoamine system may have greater efficacy than highly selective drugs, while equaling or improving their adverse effect profiles. This article reviews the properties of duloxetine, a potent and balanced **inhibitor** of **norepinephrine** and **serotonin reuptake**. Controlled studies indicate a high degree of efficacy, tolerability, and safety for duloxetine in the treatment of major depressive disorder. In particular, rapid therapeutic onset and high remission rates have been noted. Duloxetine appears to have significant benefit in the treatment of the painful physical symptoms associated with depression. The continued presence of such symptoms may predict relapse. Accordingly, it is hoped that duloxetine therapy may reduce the likelihood of depressive relapse.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't
Adrenergic Uptake Inhibitors: AE, adverse effects
Adrenergic Uptake Inhibitors: PD, pharmacology
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Clinical Trials
Depressive Disorder: DI, diagnosis
*Depressive Disorder: DT, drug therapy
Depressive Disorder: PX, psychology
Multicenter Studies
Norepinephrine: ME, metabolism
Pain: DT, drug therapy
Serotonin: ME, metabolism
Serotonin Uptake Inhibitors: AE, adverse effects
Serotonin Uptake Inhibitors: PD, pharmacology
*Serotonin Uptake Inhibitors: TU, therapeutic use
Somatoform Disorders: DT, drug therapy
Thiophenes: AE, adverse effects
Thiophenes: PD, pharmacology
*Thiophenes: TU, therapeutic use
Treatment Outcome

CAS REGISTRY NO.: 116539-58-3 (duloxetine); 50-67-9 (Serotonin); 51-41-2 (Norepinephrine)
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Serotonin Uptake Inhibitors); 0 (Thiophenes)

L57 ANSWER 10 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003433773 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12975715
TITLE: Efficacy of venlafaxine for the long term treatment of chronic pain with associated major depressive disorder.
AUTHOR: Bradley Ronald H; Barkin Robert L; Jerome John; DeYoung Kevin; Dodge Charles William
CORPORATE SOURCE: Total Health Care of Michigan, P.C., East Lansing, MI 48823, USA.. rhbradley@msn.com
SOURCE: American journal of therapeutics, (2003 Sep-Oct) 10 (5) 318-23.
Journal code: 9441347. ISSN: 1075-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20030917
Last Updated on STN: 20040207
Entered Medline: 20040206

ABSTRACT:
BACKGROUND: This was an open-label, single-center study of the long-term efficacy and effectiveness of venlafaxine extended release (XR) in the treatment of chronic pain and depression in outpatients. All patients have been diagnosed with major depressive disorder (MDD) of various types, with or without chronic pain, and had previously failed treatment with either tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs). METHODS: Efficacy of treatment was determined using the 21-item Hamilton Rating Scale for Depression (HAMD-21), the Visual Analogue Scale (VAS) for the evaluation of pain, and a 12-item quality of life scale (QOL). Patients were treated in an unblended open trial for 1 year with 150 mg or more of venlafaxine XR once daily. RESULTS: After 1 year of treatment, 21-item Hamilton Rating Scale for Depression, Visual Analogue Scale, and quality of life scores were significantly improved from permanent baseline scores. CONCLUSION: These data show long-term efficacy and effectiveness of venlafaxine XR, a **serotonin** (5-HT) and **norepinephrine** (NE) and dopamine (DA) **reuptake inhibitor** antidepressant agent, having analgesic properties.

CONTROLLED TERM: Check Tags: Female; Human; Male
Adult
Analgesics: AD, administration & dosage
*Analgesics: TU, therapeutic use
Antidepressive Agents, Second-Generation: AD, administration & dosage
*Antidepressive Agents, Second-Generation: TU, therapeutic use
Chronic Disease
Cyclohexanols: AD, administration & dosage
*Cyclohexanols: TU, therapeutic use
Delayed-Action Preparations
Depression, Involutional: CO, complications
*Depression, Involutional: DT, drug therapy
Pain: CO, complications
***Pain: DT, drug therapy**
Pain Measurement
Serotonin Uptake Inhibitors: AD, administration & dosage

*Serotonin Uptake Inhibitors: TU, therapeutic use
Severity of Illness Index
Time Factors
Treatment Outcome
CAS REGISTRY NO.: 93413-69-5 (venlafaxine)
CHEMICAL NAME: 0 (Analgesics); 0 (Antidepressive Agents, Second-Generation); 0 (Cyclohexanols); 0 (Delayed-Action Preparations); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 11 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003305253 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12833238
TITLE: [Fibromyalgia: a challenge for neuroscience]. Fibromialgia: un reto tambien para la neurociencia.
AUTHOR: Leza J C
CORPORATE SOURCE: Universidad Complutense. Facultad de Medicina, Madrid, Espana.. jcleza@med.ucm.es
SOURCE: Revista de neurologia, (2003 Jun 16-30) 36 (12) 1165-75. Ref: 134
Journal code: 7706841. ISSN: 0210-0010.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20030701
Last Updated on STN: 20040313
Entered Medline: 20040312

ABSTRACT:
AIMS: In this survey we present the most recent findings regarding the physiopathology and therapeutic guidelines of a disease we still know very little about: fibromyalgia. This disorder is characterized by a chronic process of generalized musculoskeletal pain accompanied by chronic fatigue, sleep disorders and, on many occasions, neuroendocrine disorders. DEVELOPMENT: Most research on the physiopathology of fibromyalgia points towards some kind of pain transmission disorder in the dorsal horn of the spinal cord. In chronic pain processes, a resonance effect is produced in the synapse of the dorsal horn and this gives rise to allodynia and hyperalgesia. From a biochemical point of view, glutamate and substance P receptors, as well as the main systems involved in the transmission of pain, serotonin and noradrenaline, seem to play a fundamental role. Patients with fibromyalgia have generally been seen to have lowered 5HT activity and an increase in substance P. In addition to these alterations in the perception of pain, serotonin could also be responsible for the frequently occurring sleep, hormone and neuropsychiatric disorders observed in these patients. CONCLUSIONS: Nowadays fibromyalgia is still a challenge for modern medicine. Indeed, the neuroscientific community must design a basic scientific approach carried out at the patient s bedside in order to find pharmacological tools with which to relieve these symptoms. Of the extensive therapeutic arsenal that has been tested in these patients to date, classical antidepressants and **serotonin** and ***noradrenaline*** **reuptake inhibitors**, used in sub antidepressant doses, seem to be the most effective.
CONTROLLED TERM: Check Tags: Human
Antidepressive Agents: TU, therapeutic use
Disease Progression
English Abstract
Fibromyalgia: DI, diagnosis
Fibromyalgia: EP, epidemiology
***Fibromyalgia: PP, physiopathology**
***Fibromyalgia: TH, therapy**

Neural Pathways: CY, cytology
Neural Pathways: ME, metabolism
Neurosecretory Systems: PH, physiology
Neurotransmitters: ME, metabolism
Pain: ME, metabolism
Sleep: PH, physiology
CHEMICAL NAME: 0 (Antidepressive Agents); 0 (Neurotransmitters)

L57 ANSWER 12 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003273025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12798668
TITLE: Evaluation of the anti-inflammatory and anti-nociceptive effects of different antidepressants in the rat.
AUTHOR: Abdel-Salam Omar M E; Nofal Salwa M; El-Shenawy Siham M
CORPORATE SOURCE: Department of Pharmacology, National Research Centre, Tahrir Street, Dokki, Cairo, Egypt.. omasalam@hotmail.com
SOURCE: Pharmacological research : official journal of the Italian Pharmacological Society, (2003 Aug) 48 (2) 157-65. Journal code: 8907422. ISSN: 1043-6618.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20030612
Last Updated on STN: 20031218
Entered Medline: 20040624

ABSTRACT:
The present study was designed to compare the anti-inflammatory and anti-nociceptive effects of different classes of antidepressant drugs on the carrageenan paw oedema and tail-electric stimulation assays in the rat. Drugs were intraperitoneally administered 30 min prior to carrageenan or nociceptive testing. The non-selective **noradrenaline** (NA) and **serotonin** (5-HT) **reuptake inhibitors** imipramine, amitriptyline and clomipramine displayed anti-inflammatory activity in the carrageenan model of paw inflammation. The maximal degree of oedema inhibitions seen with these agents were 28.8, 41.5 and 46.8% for 5, 10 and 20 mg kg(-1) amitriptyline, 26.2, 38.2 and 51.4% for 3.75, 7.5 and 15 mg kg(-1) imipramine and 51.2 and 54.1% for 16 and 32 mg kg(-1) clomipramine, respectively. The heterocyclic agent trazodone significantly inhibited paw oedema by 46 and 41% at 1 and 2h after dosing at the highest dose (40 mg kg(-1)) examined. Fluoxetine, a selective 5-HT reuptake inhibitor (SSRI) caused dose-related reduction of paw oedema, with 20.7% inhibition at the dose of 10 mg kg(-1). In contrast, sertraline, another SSRI caused dose-dependent enhancement of paw oedema. All antidepressant drugs in the study showed anti-nociceptive properties in the tail-electric stimulation assay with amitriptyline and trazodone being the most effective in this respect. Taken together, data in the present study confirm anti-inflammatory and anti-nociceptive effect for some antidepressant drugs and indicate that SSRIs differently affects inflammation.
CONTROLLED TERM: Check Tags: Male
Amitriptyline: TU, therapeutic use
Analysis of Variance
Animals
*Antidepressive Agents: TU, therapeutic use
Carrageenan
Clomipramine: TU, therapeutic use
Disease Models, Animal
Dose-Response Relationship, Drug
Drug Evaluation, Preclinical
Electroshock
Fluoxetine: TU, therapeutic use

Imipramine: TU, therapeutic use
Inflammation: CI, chemically induced
*Inflammation: DT, drug therapy
***Pain: DT, drug therapy**
Pain Measurement
Rats
Rats, Sprague-Dawley
Sertraline: TU, therapeutic use
Trazodone: TU, therapeutic use

CAS REGISTRY NO.: 19794-93-5 (Trazodone); 303-49-1 (Clomipramine); 50-48-6 (Amitriptyline); 50-49-7 (Imipramine); 54910-89-3 (Fluoxetine); 79617-96-2 (Sertraline); 9000-07-1 (Carrageenan)
CHEMICAL NAME: 0 (Antidepressive Agents)

L57 ANSWER 13 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003249791 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12773276
TITLE: Management of fibromyalgia.
AUTHOR: Patkar Ashwin A; Bilal Louai; Masand Prakash S
CORPORATE SOURCE: Department of Psychiatry, Thomas Jefferson University, 833 Chestnut Street, Suite 210E, Philadelphia, PA 19107, USA.. ashwin.patkar@mail.tju.edu
SOURCE: Current psychiatry reports, (2003 Jul) 5 (3) 218-24. Ref: 62
Journal code: 100888960. ISSN: 1523-3812.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030530
Last Updated on STN: 20040117
Entered Medline: 20040116

ABSTRACT:
Fibromyalgia is characterized by widespread pain, persistent fatigue, nonrestorative sleep, and generalized morning stiffness. The diagnosis is based on patients' reports of pain and fatigue, clinical findings of multiple tender points, and exclusion of a range of connective tissue and other medical disorders. Treatment of fibromyalgia is multidisciplinary with an emphasis on active patient participation, medications, cognitive behavioral therapy, and physical modalities. No single medication has been found to effectively control all the symptoms, and a rational combination of different medications is often necessary. Currently available medication classes include the selective **serotonin uptake inhibitors**, the ***serotonin*** and **norepinephrine reuptake** ***inhibitors*** , tricyclic antidepressants, analgesics, hypnotic agents, and anticonvulsants. Treatment modalities should be individualized for patients based on target symptoms and impairment in functioning. As is the case with several chronic disorders, the treatment is often prolonged and improvement may occur slowly. Patience and positive attitude on part of the physician and active involvement of patients and their families in treatment are likely to enhance improvement.

CONTROLLED TERM: Check Tags: Human
Combined Modality Therapy
***Fibromyalgia: DI, diagnosis**
Fibromyalgia: ET, etiology
Fibromyalgia: TH, therapy
Pain Measurement
Patient Care Team

Patient Participation
Prognosis

L57 ANSWER 14 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003233984 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12755646
TITLE: Physical symptoms of depression: unmet needs.
AUTHOR: Greden John F
CORPORATE SOURCE: Department of Psychiatry and University of Michigan Depression Center, Ann Arbor, MI 48109, USA.. gredenj@umich.edu
SOURCE: Journal of clinical psychiatry, (2003) 64 Suppl 7 5-11. Ref: 31
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030521
Last Updated on STN: 20030702
Entered Medline: 20030701

ABSTRACT:
The burden of depression on society is sizable. Innate to this burden are underdiagnosis and under-treatment of unipolar and bipolar major depressive disorder in all parts of the health care system in part due to underrecognition of the physical symptoms that commonly are core components of major depressive disorder. Physical pains especially complicate the diagnosis of depression. Many patients de-emphasize psychosocial symptoms while emphasizing pains as their primary or sole complaints. There is a high correlation between the number of physical symptoms reported and the presence of depression. Additionally, patients with residual physical and emotional symptoms following treatment for depression appear to be at higher risk of relapse compared with those who have no residual symptoms. Complex genetic vulnerabilities underlie the depressive diathesis, and stress appears to be an accentuation for the gene expression that sets off episodes of depression in persons with these predispositions. If underdiagnosis interferes and acute treatment is not implemented early and effectively for initial episodes of depression and maintained after remission, individuals with genetic vulnerabilities may experience a pattern of recurrences, cycle acceleration, and increased severity. Serotonin and norepinephrine may be shared neurochemical links that tie depression and physical symptoms together. Thus, it is reasonable to hypothesize that antidepressants that incorporate both **serotonin** and ***norepinephrine*** **reuptake inhibition** might be a more efficacious treatment approach for patients with physical symptoms of depression.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human; Male
Adolescent
Adrenergic Uptake Inhibitors: TU, therapeutic use
Adult
Comorbidity
Cost of Illness
*Delivery of Health Care
*Depressive Disorder: DI, diagnosis
Depressive Disorder: DT, drug therapy
Depressive Disorder: EP, epidemiology
Health Care Costs
Norepinephrine
Pain: DI, diagnosis
Pain: EP, epidemiology

Primary Health Care: ST, standards
Recurrence
Serotonin Uptake Inhibitors: TU, therapeutic use
Treatment Outcome
CAS REGISTRY NO.: 51-41-2 (Norepinephrine)
CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 15 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003222427 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12665411
TITLE: Emerging trends in the pharmacotherapy of chronic pain.
AUTHOR: Nitu A N; Wallihan R; Skljarevski V; Ramadan N M
CORPORATE SOURCE: Finch University of Health Sciences/Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064-3095, USA.
SOURCE: Expert opinion on investigational drugs, (2003 Apr) 12 (4) 545-59. Ref: 101
Journal code: 9434197. ISSN: 1354-3784.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030515
Last Updated on STN: 20030611
Entered Medline: 20030610
ABSTRACT:
The pharmacotherapy for pain is dominated by conventional analgesics such as the opioids and the non-steroidal anti-inflammatory drugs. Recent advances in the understanding of the mechanisms of pain in general and chronic pain in particular, opened the field of analgesic therapy to newer pharmacological targets, which are aimed at improved efficacy and enhanced tolerability over conventional antipain treatments. Many novel targets are still in preclinical development, but some have made it into human trials and have shown promise. Newer anticonvulsants, new generation cyclooxygenase inhibitors, better tolerated glutamate modulators and balanced **serotonin/***noradrenaline*** re-**uptake inhibitors** are some targets that have shown promise in the clinic. These and other compounds that are in advanced phases of development for chronic pain are reviewed in this paper. It is hoped that the decade of pain control and research will lead us to an arsenal of effective and safe analgesics that will conquer the problem of chronic pain.
CONTROLLED TERM: Check Tags: Human
*Analgesics: TU, therapeutic use
Animals
Anti-Inflammatory Agents: TU, therapeutic use
Calcium Channel Blockers: TU, therapeutic use
Cannabinoids: TU, therapeutic use
Chronic Disease
***Pain: DT, drug therapy**
Pain: ME, metabolism
Sodium Channel Blockers: TU, therapeutic use
CHEMICAL NAME: 0 (Analgesics); 0 (Anti-Inflammatory Agents); 0 (Calcium Channel Blockers); 0 (Cannabinoids); 0 (Sodium Channel Blockers)

L57 ANSWER 16 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2003207026 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12727329
TITLE: The antihyperalgesic effect of venlafaxine in diabetic rats

does not involve the opioid system.

AUTHOR: Marchand Fabien; Alloui Abdelkrim; Chapuy Eric; Hernandez Alejandro; Pelissier Teresa; Ardid Denis; Eschalier Alain

CORPORATE SOURCE: E 9904 INSERM/UdA, Laboratoire de Pharmacologie Medicale, Faculte de Medecine, 63001 Cedex 1, Clermont-Ferrand, France.

SOURCE: Neuroscience letters, (2003 May 15) 342 (1-2) 105-8. Journal code: 7600130. ISSN: 0304-3940.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200307

ENTRY DATE: Entered STN: 20030503
Last Updated on STN: 20030801
Entered Medline: 20030731

ABSTRACT:
Venlafaxine (VFX) is a structurally novel antidepressant that **inhibits** ***reuptake*** of **serotonin** and **norepinephrine** but, unlike tricyclic antidepressants, has few side effects. The present work studies the antihyperalgesic effect of repeated administrations of VFX (five successive injections of 2.5, 5 or 10 mg/kg, s.c., every half-life) in diabetic rats with the paw pressure test and the effect of the opioid receptor antagonist naloxone (1 mg/kg, i.v.) because an opioidergic mechanism is usually considered to be involved in the analgesic effect of antidepressants. VFX induced a significant dose-dependent increase in vocalization thresholds. This effect was not reversed by naloxone. Thus, we demonstrate a clear antinociceptive effect of VFX which, unlike that of most mixed tricyclic antidepressants, does not involve the endogenous opioid system.

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
*Analgesics: PD, pharmacology
Animals
*Cyclohexanols: PD, pharmacology
Diabetes Mellitus: CO, complications
Dose-Response Relationship, Drug
*Hyperalgesia: DT, drug therapy
Hyperalgesia: ET, etiology
*Naloxone: PD, pharmacology
*Narcotic Antagonists: PD, pharmacology
***Pain Threshold: DE, drug effects**
Pressure
Rats
Rats, Sprague-Dawley
Vocalization, Animal: DE, drug effects

CAS REGISTRY NO.: 465-65-6 (Naloxone); 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Analgesics); 0 (Cyclohexanols); 0 (Narcotic Antagonists)

L57 ANSWER 17 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2003188620 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12707430

TITLE: Venlafaxine versus imipramine in painful polyneuropathy: a randomized, controlled trial.

AUTHOR: Sindrup S H; Bach F W; Madsen C; Gram L F; Jensen T S

CORPORATE SOURCE: Department of Neurology, University Hospitals, Odense, Denmark.. s.sindrup@dadlnet.dk

SOURCE: Neurology, (2003 Apr 22) 60 (8) 1284-9. Journal code: 0401060. ISSN: 1526-632X.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030423
Last Updated on STN: 20040115
Entered Medline: 20040114

ABSTRACT:
BACKGROUND: Tricyclic antidepressants (TCA) are often used in the treatment of painful polyneuropathy. Venlafaxine is a **serotonin** and weak ***noradrenaline*** **reuptake inhibitor** antidepressant with a different profile of other pharmacologic actions from those of TCA. OBJECTIVE: To test if venlafaxine would relieve painful polyneuropathy and compare its possible efficacy with that of the TCA imipramine. METHODS: The study design was randomized, double blind, and placebo controlled, with a three-way crossover. Forty patients were assigned to one of the treatment sequences, and 29 completed all three study periods. The daily doses were venlafaxine 225 mg and imipramine 150 mg. During the three treatment periods, each of 4 weeks' duration, patients rated pain paroxysms, constant pain, and touch- and pressure-evoked pain by use of 0- to 10-point numeric rating scales. RESULTS: The sum of the individual pain scores during treatment week 4 was lower on venlafaxine (80% of baseline score; p = 0.006) and imipramine (77%; p = 0.001) than on placebo (100%) and did not show any statistical difference between venlafaxine and imipramine (p = 0.44). The individual pain scores for pain paroxysms, constant pain, and pressure-evoked pain showed a similar pattern, whereas touch-evoked pain was uncommon and was not altered by any of the drugs. Numbers needed to treat to obtain one patient with moderate or better pain relief were 5.2 for venlafaxine and 2.7 for imipramine. CONCLUSION: Venlafaxine relieves pain in polyneuropathy and may be as effective as imipramine.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
*Analgesics, Non-Narcotic: TU, therapeutic use
Cross-Over Studies
*Cyclohexanols: TU, therapeutic use
Diabetic Neuropathies: DT, drug therapy
Double-Blind Method
*Imipramine: TU, therapeutic use
Middle Aged
***Neuralgia: DT, drug therapy**
*Neurotransmitter Uptake Inhibitors: TU, therapeutic use
Norepinephrine: ME, metabolism
Pain Measurement
*Polyneuropathies: DT, drug therapy
Pressure: AE, adverse effects
Serotonin: ME, metabolism
Touch
Treatment Outcome

CAS REGISTRY NO.: 50-49-7 (Imipramine); 50-67-9 (Serotonin); 51-41-2 (Norepinephrine); 93413-69-5 (venlafaxine)
CHEMICAL NAME: 0 (Analgesics, Non-Narcotic); 0 (Cyclohexanols); 0 (Neurotransmitter Uptake Inhibitors)

L57 ANSWER 18 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2002481810 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12243607
TITLE: Nefopam abuse.
AUTHOR: Villier Celine; Mallaret Michel P
CORPORATE SOURCE: Centre d'Evaluation et d'Information sur la Pharmacodependance de Grenoble, Grenoble, France.. CVillier@chu-grenoble.fr
SOURCE: Annals of pharmacotherapy, (2002 Oct) 36 (10) 1564-6.

Journal code: 9203131. ISSN: 1060-0280.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20020924
Last Updated on STN: 20030426
Entered Medline: 20030425

ABSTRACT:
OBJECTIVE: To report 3 patients who abused nefopam, a central analgesic that ***inhibits*** **serotonin**, **norepinephrine**, and dopamine ***reuptake*** . CASE SUMMARIES: CASE 1: A 42-year-old white woman with migraines started nefopam therapy about 10 years ago. She now obtains nefopam by prescription forgery and self-administers intramuscular nefopam 300 mg/d. She experiences anticholinergic effects of nefopam and, when attempting withdrawal, depressive symptoms. CASE 2: A 40-year-old white woman with osteoporosis has injected 120 mg of nefopam intramuscularly daily for several years. When she tried to increase doses due to worsening of her symptoms, she experienced tremor, involuntary movements, and dry mouth, and became aggressive. She then resumed the initial doses. She now reports symptoms of depression when attempting withdrawal. CASE 3: A 33-year-old white man, with a history of alcohol and benzodiazepine dependence and ileostomy, and an implanted drug delivery system, has been prescribed nefopam. Fifteen days after therapy was initiated, his daily consumption was 840 mg/d, and further increased to 1840 mg/d. He experienced violent behavior, agitation, facial dysesthesia and myoclonus, tremor of fingers, and sweating. He did not attempt withdrawal. DISCUSSION: The patients described above are drug-dependent according to the Diagnostic and Statistical Manual, 4th Edition. All patients developed a pharmacodynamic tolerance phenomenon, which can develop rapidly. Violent behavior, tremor after massive intake, and depressive symptoms during withdrawal are similar to those reported with psychostimulant abuse. CONCLUSIONS: When abused, nefopam has primarily psychostimulant-like effects, which are probably linked to its dopamine reuptake inhibition properties.
CONTROLLED TERM: Check Tags: Female; Human; Male
Adult
*Analgesics, Non-Narcotic: AD, administration & dosage
Injections, Intramuscular
Injections, Intravenous
*Nefopam: AD, administration & dosage
Pain: DT, drug therapy
*Substance-Related Disorders: ET, etiology
CAS REGISTRY NO.: 13669-70-0 (Nefopam)
CHEMICAL NAME: 0 (Analgesics, Non-Narcotic)

L57 ANSWER 19 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2002269539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11978164
TITLE: Ziprasidone: the fifth atypical antipsychotic.
AUTHOR: Caley Charles F; Cooper Chandra K
CORPORATE SOURCE: School of Pharmacy, University of Connecticut, Storrs, CT, USA.. ccaley4@netscape.net
SOURCE: Annals of pharmacotherapy, (2002 May) 36 (5) 839-51. Ref: 41
Journal code: 9203131. ISSN: 1060-0280.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020516
Last Updated on STN: 20021019
Entered Medline: 20021018

ABSTRACT:
OBJECTIVE: To review the pharmacology, pharmacokinetics, clinical efficacy, and adverse effects of ziprasidone as a treatment for schizophrenia. DATA SOURCES: Information was selected from a MEDLINE search (July 2000-October 2001) of English-language medical literature using ziprasidone as the search term. Manual searches of pertinent journal article references, request for medical information from Pfizer, and access of the Web site of the Food and Drug Administration were also performed. STUDY SELECTION: All available published information regarding the pertinent characteristics of ziprasidone were considered for selection. DATA EXTRACTION: Pharmacology and pharmacokinetic studies were selected to provide a comprehensive description of these characteristics. Clinical investigations were evaluated for design, sample size, diagnosis, duration, and outcome. Data from all investigations were selected by 1 author and reviewed by both authors. DATA SYNTHESIS: Ziprasidone is a benzisothiazolyl piperazine-type atypical antipsychotic that shares the serotonin(2A)/dopamine(2) (5-HT(2A)/D(2)) profile of the available atypical antipsychotics. Ziprasidone has demonstrated in.vitro activity as a 5-HT(1A) receptor agonist and as a very weak **inhibitor** of **serotonin** and **norepinephrine reuptake**. These data do not support ziprasidone as being a clinically meaningful **inhibitor** of ***serotonin*** /**norepinephrine reuptake**. Oral bioavailability of ziprasidone taken with food is approximately 60%, half-life is approximately 6-7 hours, and protein binding is extensive at >99%. Twelve metabolites have been identified, yet only 4 of these are considered to be primary metabolites. Metabolism of ziprasidone by aldehyde oxidase produces its only metabolite with potential pharmacologic activity; CYP3A4 also contributes to the metabolism of ziprasidone. Clinical studies support ziprasidone as efficacious for the treatment of patients with acute exacerbations of schizophrenia or schizoaffective disorder. Daily doses permitted in these clinical trials ranged from 40 to 160 mg, but only doses between 120 and 160 mg/d have been superior to placebo. Future research efforts should be directed toward refractory schizophrenia, cognitive impairment in schizophrenia, affective and anxiety symptoms associated with schizoaffective disorder, and bipolar disorder. Adverse effect characteristics of ziprasidone commonly include headache, nausea, and somnolence; infrequent effects include extrapyramidal symptoms and weight gain. Ziprasidone has been reported to cause an average QTc prolongation of approximately 20 msec; there have only been 2 patients (0.06%) reported by the manufacturer to have a measured QTc interval >500 msec. CONCLUSIONS: Ziprasidone is a safe and efficacious atypical antipsychotic for the acute management of schizophrenia. Efficacy data and most safety data for ziprasidone support its use as a first-line treatment for schizophrenia; however, its potential effects on ventricular repolarization relegate it to second-line status in patients with comorbid cardiovascular risks.

CONTROLLED TERM: Check Tags: Comparative Study; Human
Acute Disease
Antipsychotic Agents: AD, administration & dosage
Antipsychotic Agents: PK, pharmacokinetics
*Antipsychotic Agents: TU, therapeutic use
Basal Ganglia Diseases: CI, chemically induced
Body Weight: DE, drug effects
Headache: CI, chemically induced
Injections, Intramuscular
Long QT Syndrome: CI, chemically induced
Nausea: CI, chemically induced
Piperazines: AE, adverse effects
Piperazines: PK, pharmacokinetics
*Piperazines: TU, therapeutic use

Randomized Controlled Trials
Schizophrenia: DT, drug therapy
Thiazoles: AE, adverse effects
Thiazoles: PK, pharmacokinetics
*Thiazoles: TU, therapeutic use
Treatment Outcome
Weight Gain: DE, drug effects
CAS REGISTRY NO.: 146939-27-7 (ziprasidone)
CHEMICAL NAME: 0 (Antipsychotic Agents); 0 (Piperazines); 0 (Thiazoles)

L57 ANSWER 20 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2002259683 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12000200
TITLE: Does depression hurt?.
AUTHOR: Stahl Stephen M
CORPORATE SOURCE: Neuroscience Education Institute in Carlsbad, CA 92009, USA.
SOURCE: Journal of clinical psychiatry, (2002 Apr) 63 (4) 273-4. Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020510
Last Updated on STN: 20020602
Entered Medline: 20020531
ABSTRACT:
Depression is an illness that causes symptoms in both the body and the brain, i.e., painful physical as well as emotional and vegetative symptoms. Ascending serotonergic and noradrenergic pathways may mediate the emotional and vegetative symptoms of depression and can potentially be targets of ***serotonin*** and **norepinephrine reuptake** ***inhibitors*** to obtain relief of these symptoms. Descending serotonergic and noradrenergic pathways may regulate the painful physical symptoms of depression, and when targeted by **serotonin** and **norepinephrine** ***reuptake*** **inhibitors**, relieve these symptoms as well. Selective serotonin reuptake inhibitors have a remission rate of 35%, and dual-action reuptake inhibitors have a 45% remission rate. Despite these results, the best treatment of depression currently recognizes the 3 types of symptoms and targets them all for complete remission no matter which drug is used.
CONTROLLED TERM: Check Tags: Human
*Affective Symptoms: DI, diagnosis
Affective Symptoms: DT, drug therapy
Affective Symptoms: PP, physiopathology
Antidepressive Agents: PD, pharmacology
Antidepressive Agents: TU, therapeutic use
*Depressive Disorder: DI, diagnosis
Depressive Disorder: DT, drug therapy
Depressive Disorder: PP, physiopathology
Norepinephrine: PH, physiology
***Pain: DI, diagnosis**
Pain: DT, drug therapy
Pain: PP, physiopathology
Serotonin: PH, physiology
Serotonin Uptake Inhibitors: PD, pharmacology
Serotonin Uptake Inhibitors: TU, therapeutic use
CAS REGISTRY NO.: 50-67-9 (Serotonin); 51-41-2 (Norepinephrine)
CHEMICAL NAME: 0 (Antidepressive Agents); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 21 OF 36 MEDLINE on STN

BACKGROUND: Venlafaxine is a potent neuronal **serotonin** and ***noradrenaline*** re-**uptake inhibitor**, and to a lesser extent an inhibitor of dopamine reuptake. Paroxetine is a potent selective inhibitor of serotonin reuptake. CASE REPORT: A 27-year-old man ingested 1987.5 mg of venlafaxine and 360 mg of paroxetine. He subsequently developed systolic and diastolic hypertension, transient electrocardiographic abnormalities, and an area of persistent myocardial damage. He recovered from his overdose with his blood pressure and electrocardiogram returning to normal. The area of myocardial damage was documented on echocardiogram as an area of marked hypokinesia at the basal anterior septum. Despite the absence of confirming blood levels or the absolute exclusion of cocaine, this case indicates that venlafaxine and paroxetine have the potential for serious cardiotoxicity when taken in overdose.

CONTROLLED TERM: Check Tags: Human; Male
Adult
Anti-Arrhythmia Agents
Chest Pain: CI, chemically induced
*Cyclohexanols: PO, poisoning
Electrocardiography
*Heart: DE, drug effects
Hypertension: CI, chemically induced
Hypertrophy, Left Ventricular: CI, chemically induced
*Myocardial Diseases: CI, chemically induced
*Myocardial Diseases: DI, diagnosis
*Paroxetine: PO, poisoning
*Serotonin Uptake Inhibitors: PO, poisoning
Tachycardia, Sinus: CI, chemically induced
Ventricular Function, Left: DE, drug effects

CAS REGISTRY NO.: 61869-08-7 (Paroxetine); 93413-69-5 (venlafaxine)

CHEMICAL NAME: 0 (Anti-Arrhythmia Agents); 0 (Cyclohexanols); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 26 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2000226400 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10763190

TITLE: [Venlafaxine withdrawal syndrome: report of six cases and review of the literature].
Syndrome de sevrage a l'arret de la venlafaxine: a propos de six cas et revue de la litterature.

AUTHOR: Pinzani V; Ginies E; Robert L; Peyriere H; Abbar M; Blayac J P

CORPORATE SOURCE: Centre regional de pharmacovigilance, CHU de Montpellier, Montpellier, France.

SOURCE: La Revue de medecine interne / fondee ... par la Societe nationale francaise de medecine interne, (2000 Mar) 21 (3) 282-4. Ref: 10
Journal code: 8101383. ISSN: 0248-8663.

PUB. COUNTRY: France

DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200004

ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000427

ABSTRACT:
INTRODUCTION: Venlafaxine is an antidepressant that selectively ***inhibits*** **serotonin reuptake** and is a ***norepinephrine*** **inhibitor**. Withdrawal syndromes can occur

after abrupt drug discontinuation of long-term regimens. EXEGESIS: We report six cases of withdrawal symptoms after venlafaxine discontinuation. CONCLUSION: Physicians must be aware of the frequency, rapidity and potent severity of these withdrawal syndromes.
CONTROLLED TERM: Check Tags: Female; Human; Male
Adult
Akathisia, Drug-Induced: ET, etiology
*Antidepressive Agents, Second-Generation: AE, adverse effects
*Cyclohexanols: AE, adverse effects
Depressive Disorder: DT, drug therapy
English Abstract
Fatigue: CI, chemically induced
Gastrointestinal Diseases: CI, chemically induced
Hallucinations: CI, chemically induced
Headache: CI, chemically induced
Middle Aged
Paresthesia: CI, chemically induced
*Serotonin Uptake Inhibitors: AE, adverse effects
Substance Withdrawal Syndrome: DI, diagnosis
*Substance Withdrawal Syndrome: ET, etiology
Time Factors
CAS REGISTRY NO.: 93413-69-5 (venlafaxine)
CHEMICAL NAME: 0 (Antidepressive Agents, Second-Generation); 0 (Cyclohexanols); 0 (Serotonin Uptake Inhibitors)

L57 ANSWER 27 OF 36 MEDLINE on STN
ACCESSION NUMBER: 1999110372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9895081
TITLE: The antinociceptive effects of morphine, desipramine, and serotonin and their combinations after intrathecal injection in the rat.
COMMENT: Erratum in: Anesth Analg 1999 Jun;88(6):1231
AUTHOR: Reimann W; Schlutz H; Selve N
CORPORATE SOURCE: Grunenthal GmbH, Department of Pharmacology, Aachen, Germany.
SOURCE: Anesthesia and analgesia, (1999 Jan) 88 (1) 141-5. Journal code: 1310650. ISSN: 0003-2999.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 20000303
Entered Medline: 19990129
ABSTRACT:
Antinociception can be produced at the spinal level by activation of opioidergic, noradrenergic, and serotonergic systems. We tested the antinociceptive effects of combined activation of all three systems. Antinociception was assessed in the rat tail-flick test, and drugs were administered via an intrathecal catheter. Morphine, the **norepinephrine** ***uptake*** **inhibitor** desipramine, and **serotonin** produced antinociception of their own. The combination of subthreshold doses of morphine 1 microg and of desipramine 3 microg produced pronounced antinociception that was antagonized by yohimbine. The combination of subthreshold morphine with serotonin 50 microg or desipramine with serotonin caused only small antinociceptive effects. When morphine combined with desipramine was decreased to a subthreshold dose, we observed pronounced antinociception when a subthreshold dose of serotonin was added. A complex interaction can be supposed by results obtained with antagonists. The activation of all three neurotransmitter systems with small doses of agonists

little risk of abuse or dependence. It therefore seemed appropriate to further investigate the efficacy and tolerability of tramadol, defined as having only weak potency, in comparison with a widely used opioid, in oncological pain. Buprenorphine was selected as an opioid with a potency equivalent to half that of morphine, but with tolerability that is partially limited by the fact that it frequently gives rise to adverse reactions considered typical of stronger opioids. To compare the analgesic effect and tolerability of tramadol and buprenorphine, 60 patients (44 men, 16 women; average age 61.4 years), all presenting with advanced tumours, were treated orally in a controlled crossover trial with randomised sequences. Patients took both drugs, each for a week, with a 24-hour washout period between treatments. Tramadol was prescribed at the daily dose of 300mg, orally, and buprenorphine at 0.6 mg/day, as a sublingual preparation. Assessments were made of Karnofsky performance status and severity of pain before and during the 4 hours after taking the 2 drugs. Each patient also completed a daily diary recording the severity of pain 1 hour after the dose, the evolution of pain during the day and its severity compared with that on the previous day. They also assessed the duration and quality of sleep. The Karnofsky index changed little with either treatment, but all other variables showed worthwhile improvement, indicating the significant analgesic effect of both drugs. Buprenorphine and tramadol had a similar analgesic effect, although the improvement with the test drug was significant within 1 hour of administration ($p < 0.05$ compared with baseline) and more marked ($p < 0.05$ on day 2 compared with buprenorpine). At the end of tramadol treatment, sleep had also improved, both quantitatively and qualitatively (both $p < 0.05$). The final assessment was significantly in favour of tramadol as regards efficacy ($p < 0.05$) and patient acceptability ($p < 0.01$). Thus, tramadol was better tolerated than buprenorphine, and caused fewer and milder adverse reactions. Only 1 patient discontinued tramadol, compared with 18 using reference therapy. Tramadol, although theoretically less potent, nevertheless brought about as much pain relief as the comparator opioid. In conclusion, for this class of drug, tramadol provides an excellent balance between efficacy and tolerability, confirming preliminary studies.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human; Male
Aged
Aged, 80 and over
Analgesics, Opioid: AE, adverse effects
*Analgesics, Opioid: TU, therapeutic use
Analysis of Variance
Buprenorphine: AE, adverse effects
*Buprenorphine: TU, therapeutic use
English Abstract
Middle Aged
*Neoplasms: CO, complications
***Pain: DT, drug therapy**
Pain: ET, etiology
Tramadol: AE, adverse effects
*Tramadol: TU, therapeutic use

CAS REGISTRY NO.: 27203-92-5 (Tramadol); 52485-79-7 (Buprenorphine)
CHEMICAL NAME: 0 (Analgesics, Opioid)

L57 ANSWER 30 OF 36 MEDLINE on STN
ACCESSION NUMBER: 97274804 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9190323
TITLE: [Treatment of post-herpes zoster pain with tramadol. Results of an open pilot study versus clomipramine with or without levomepromazine].
Traitement des douleurs post-zosteriennes par le tramadol. Resultats d'une etude pilote ouverte versus clomipramine avec ou sans levomepromazine.
AUTHOR: Gobel H; Stadler T
CORPORATE SOURCE: Service de Neurologie, Hopital Universitaire, Kiel, Allemagne.

SOURCE: Drugs, (1997) 53 Suppl 2 34-9.
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19990129
Entered Medline: 19970619

ABSTRACT:
To date, no universally applicable recommendations are available for the treatment of patients with postherpetic neuralgia. A mixture of clinical anecdotes, experimental findings and observations from clinical trials form the basis of the medical arsenal for this condition. Tricyclic antidepressants are commonly used, and clinical experience and several investigations have documented their effectiveness. Today, single entity antidepressants, which can be combined with neuroleptics to increase analgesia, are generally recommended for the treatment of postherpetic neuralgia. Some authors also recommend the additional administration of an opioid if analgesia is inadequate. Just over a decade ago, opioids were considered ineffective for the treatment of neuropathic pain; however, more recent investigations relating to the use of opioids, primarily in the treatment of nontumour-related chronic pain, have led to a revision of their use in neuropathic pain. Nevertheless, the use of opioid therapy for neurogenic pain remains controversial. Tramadol is a synthetic, centrally acting analgesic with both opioid and nonopioid analgesic activity. The nonopioid component is related to the ***inhibition*** of **noradrenaline** (**norepinephrine**) ***reuptake*** and stimulation of **serotonin** (5-hydroxytryptamine; 5-HT) release at the spinal level. In this regard, there are parallels with antidepressants, which are believed to potentiate the effect of biogenic amines in endogenous pain-relieving systems. There is evidence that, in tramadol, both mechanisms act synergistically with respect to analgesia. The aim of this pilot study was to investigate, for the first time, the analgesic efficacy and tolerability of tramadol, compared with the antidepressant clomipramine, in the treatment of postherpetic neuralgia. If necessary, clomipramine was used in combination with the neuroleptic levomepromazine. The study allowed individualised dosages at predetermined intervals up to a maximum daily dose of tramadol 600mg and clomipramine 100mg, or clomipramine 100mg with or without levomepromazine 100mg. 21 (60%) of 35 randomised patients (> or = 65 years) received the study medication over the 6-week period [tramadol n = 10; clomipramine with or without levomepromazine) n = 11]. After 3 weeks' treatment the dosage in both groups remained almost constant for the rest of the 6-week treatment phase (mean daily dose: tramadol 250 to 290mg; clomipramine 59.1 to 63.6mg). Only 3 patients required the combination of clomipramine and levomepromazine. At the outset, both groups recorded an average pain level of 'moderate' to 'very severe'. In correlation with increasing the study medication, this had decreased to 'slight' by the end of the treatment, when 9 of 10 patients in the tramadol group and of 6 of 11 patients in the clomipramine group retrospectively rated their analgesia as excellent, good or satisfactory. The psychological/physical condition of the patients did not change significantly during tramadol treatment. Sensitivity and depression parameters decreased in the clomipramine group. The incidence of adverse events for all patients was similar in both groups (tramadol 76.5%; clomipramine with or without levomepromazine 83.3%). In conclusion, tramadol would appear to be an interesting therapeutic alternative for pain relief in postherpetic neuralgia, particularly in patients who are not depressed. In clinical practice, tramadol and clomipramine can best be used differentially. For example, tramadol could be the drug of first choice in patients with obvious cardiovascular disease (not an uncommon problem in the > or = 65 year

trial investigating the prophylactic effect of amitriptyline, the selective serotonin re-uptake inhibitor citalopram, and placebo. ES2 duration was significantly shorter during treatment with amitriptyline than during placebo, P = 0.02, while ES2 duration only tended to be shorter during treatment with citalopram, P = 0.34. ES2 was not significantly correlated to the prophylactic effect of amitriptyline or to a range of clinical and experimental pain parameters. Our results demonstrate that amitriptyline reduces ES2 and indicate that ES2 is modulated by serotonergic as well as noradrenergic neuronal pathways.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
*Amitriptyline: TU, therapeutic use
Citalopram: TU, therapeutic use
Double-Blind Method
***Headache: DT, drug therapy**
Middle Aged
*Temporal Muscle: DE, drug effects

CAS REGISTRY NO.: 50-48-6 (Amitriptyline); 59729-33-8 (Citalopram)

L57 ANSWER 34 OF 36 MEDLINE on STN
ACCESSION NUMBER: 97016326 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8862961
TITLE: A risk-benefit assessment of tramadol in the management of pain.
AUTHOR: Radbruch L; Grond S; Lehmann K A
CORPORATE SOURCE: Department of Anaesthesiology, University of Cologne, Germany.. lukas.radbruch@uni-koeln.de
SOURCE: Drug safety : an international journal of medical toxicology and drug experience, (1996 Jul) 15 (1) 8-29.
Ref: 128
Journal code: 9002928. ISSN: 0114-5916.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19980206
Entered Medline: 19970121

ABSTRACT:
Tramadol is a cyclohexanol derivative with mu-agonist activity. It has been used as an analgesic for postoperative or chronic pain since the late 1970s, and became one of the most popular analgesics of its class in Germany. International interest has been renewed during the past few years, when it was discovered that tramadol not only acts on opioid receptors, but also ***inhibits*** **serotonin** (5-hydroxytryptamine; 5-HT) and ***noradrenaline*** (norepinephrine) **reuptake**. This review aims to provide a risk-benefit assessment of tramadol in the management of acute and chronic pain syndromes. Tramadol has been used intraoperatively as part of balanced anaesthesia. Such use is under discussion, however, as it was associated with a high incidence of intraoperative recall and dreaming, and postoperative respiratory depression has been described after intraoperative administration of high doses. Postoperatively, intravenous and intramuscular tramadol has been used with good efficacy. Analgesic doses were comparable with pethidine (meperidine) and 10 times higher than morphine. Nausea and vomiting were the most frequently reported adverse effects. In controlled studies, haemodynamic and respiratory parameters were only minimally impaired. The risk of severe respiratory depression in typical dosages is negligible in comparison with other opioids used for postoperative pain management. Tramadol has been used with good results for the management of labour pain without

serum concentration of (+)-M1 2 to 10 hours after tramadol ranged from 10 to 100 ng/L in extensive metabolizers, whereas in poor metabolizers serum concentrations of (+)-M1 were below or around the detection limit of 3 ng/ml. It is concluded that formation of (+)-M1 by way of CYP2D6 is important for the effect of tramadol on experimental pain.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Analgesics, Opioid: BL, blood
Analgesics, Opioid: PK, pharmacokinetics
*Analgesics, Opioid: PD, pharmacology
Cold: AE, adverse effects
Cross-Over Studies
*Cytochrome P-450 CYP2D6: ME, metabolism
Double-Blind Method
Pain: ET, etiology
Pain: ME, metabolism
***Pain: PC, prevention & control**
***Pain Threshold: DE, drug effects**
Pressure: AE, adverse effects
Reference Values
Reflex: DE, drug effects
Sparteine: ME, metabolism
Tramadol: BL, blood
Tramadol: PK, pharmacokinetics
*Tramadol: PD, pharmacology

CAS REGISTRY NO.: 27203-92-5 (Tramadol); 90-39-1 (Sparteine)

CHEMICAL NAME: 0 (Analgesics, Opioid); EC 1.14.14.1 (Cytochrome P-450 CYP2D6)

L57 ANSWER 33 OF 36 MEDLINE on STN

ACCESSION NUMBER: 97070269 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8913195

TITLE: Amitriptyline, a combined **serotonin** and **noradrenaline** re-**uptake inhibitor**, reduces exteroceptive suppression of temporal muscle activity in patients with chronic tension-type headache.

AUTHOR: Bendtsen L; Jensen R; Olesen J

CORPORATE SOURCE: Department of Neurology, Glostrup Hospital, University of Copenhagen, Glostrup, Denmark.

SOURCE: Electroencephalography and clinical neurophysiology, (1996 Oct) 101 (5) 418-22.
Journal code: 0375035. ISSN: 0013-4694.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199612

ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961220

ABSTRACT:
Although reflexes in human jaw muscles have been extensively studied, the neurotransmitters involved in the regulation of these reflexes are not well known. The aim of the present study was to investigate whether amitriptyline, a combined **serotonin** and **noradrenaline** re-**uptake** ***inhibitor*** , modulates the late exteroceptive suppression period (ES2) of temporal muscle activity in chronic tension-type headache. ES2 was recorded with a previously evaluated method and assessed by a blinded observer in 35 patients with chronic tension-type headache. Thereafter, ES2 was recorded in 27 of these patients during a double-blind, placebo-controlled, 3-way crossover

respiratory depression of the neonate. It was also effective for the treatment of pain from myocardial ischaemia, ureteric colic and acute trauma. Good results have been published for cancer pain management with tramadol in several studies. The potential for abuse or addiction seems to be minimal, and serious complications have not been reported. For patients with severe pain, the efficacy of morphine is superior, and most patients with adequate analgesia from tramadol had to be changed to a more potent opioid after a few weeks due to increased nociceptive input during tumour progression. Tramadol can be recommended as a safe and efficient drug for step II according to the World Health Organization guidelines for cancer pain management.

CONTROLLED TERM: Check Tags: Human
Administration, Oral
Analgesics, Opioid: AD, administration & dosage
Analgesics, Opioid: AE, adverse effects
*Analgesics, Opioid: TU, therapeutic use
Animals
Central Nervous System: DE, drug effects
Digestive System: DE, drug effects
Hemodynamic Processes: DE, drug effects
Injections, Intramuscular
***Pain: DT, drug therapy**
Pain, Postoperative: DT, drug therapy
Risk Assessment
Substance-Related Disorders
Tramadol: AD, administration & dosage
Tramadol: AE, adverse effects
*Tramadol: TU, therapeutic use

CAS REGISTRY NO.: 27203-92-5 (Tramadol)
CHEMICAL NAME: 0 (Analgesics, Opioid)

L57 ANSWER 35 OF 36 MEDLINE on STN
ACCESSION NUMBER: 96350145 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8764760
TITLE: Pharmacokinetics, efficacy, and safety of analgesia with a focus on tramadol HCl.
AUTHOR: Gibson T P
CORPORATE SOURCE: Ortho-McNeil Pharmaceutical, Raritan, New Jersey 08869, USA.
SOURCE: American journal of medicine, (1996 Jul 31) 101 (1A) 47S-53S. Ref: 30
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960924
Last Updated on STN: 19960924
Entered Medline: 19960913

ABSTRACT:
Chronic pain remains a problem because it is often misdiagnosed and undertreated. Adverse effects and safety concerns associated with many analgesics have limited the use of these agents and contributed to the undertreatment of pain. With regard to the pharmacologic agents most commonly used to manage pain, centrally acting analgesics (e.g., morphine, codeine) are associated with respiratory depression, tolerance, and dependence, and most nonsteroidal anti-inflammatory drugs (NSAIDs) produce adverse gastrointestinal effects. New to the United States, tramadol HCl, which has been prescribed for almost 2 decades in Europe, is a single-entity, centrally acting analgesic that is effective for the management of moderate to moderately severe pain.

Although the mechanism of action of this analgesic is not completely understood, animal models suggest that at least two complementary modes of action appear applicable: (1) binding of parent compound and mono-O-desmethyltramadol (M1 metabolite) to the mu-opioid receptor and (2) weak ***inhibition*** of **norepinephrine** and **serotonin** ***reuptake*** . Clinical experience suggests that tramadol appears to have a low potential for abuse or addiction. Results from clinical trials conducted in the United States as well as European postmarketing surveillance studies indicate that tramadol is an effective analgesic that may have a particularly important role in the management of chronic painful conditions.

CONTROLLED TERM: Check Tags: Human
Analgesics, Opioid: AD, administration & dosage
Analgesics, Opioid: AE, adverse effects
*Analgesics, Opioid: PK, pharmacokinetics
Chronic Disease
Clinical Trials
***Pain: DT, drug therapy**
***Pain: ME, metabolism**
Tramadol: AD, administration & dosage
Tramadol: AE, adverse effects
*Tramadol: PK, pharmacokinetics

CAS REGISTRY NO.: 27203-92-5 (Tramadol)
CHEMICAL NAME: 0 (Analgesics, Opioid)

L57 ANSWER 36 OF 36 MEDLINE on STN
ACCESSION NUMBER: 89040532 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3054623
TITLE: A double-blind randomized study of clomipramine versus maprotiline in patients with idiopathic pain syndromes.
AUTHOR: Eberhard G; von Knorring L; Nilsson H L; Sundequist U; Bjorling G; Linder H; Svard K O; Tysk L
CORPORATE SOURCE: Department of Psychiatry, Malmo General Hospital, Sweden.
SOURCE: Neuropsychobiology, (1988) 19 (1) 25-34.
Journal code: 7512895. ISSN: 0302-282X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198812
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19881206

ABSTRACT:
Seventy patients with idiopathic syndromes were treated with maprotiline, a ***noradrenaline*** **reuptake inhibitor**, or clomipramine, a **serotonin reuptake inhibitor** in a 6-week, double-blind, randomized, multicenter trial. Fifty-two patients completed the double-blind phase. Overall, 50% of the patients improved. Significant decreases were seen not only in the levels of pain but also in bodily discomfort, sadness an inner tension (determined by visual analogue scales, VAS). A decrease was also found in the frequency of sleep disturbances, intellectual and emotional inhibition, irritability, guilt feelings, retardation, sadness and suicidal ideas (observed ratings). Sixty-three percent of the subjects showed an overall improvement during treatment with clomipramine as compared to 36% during treatment with maprotiline (p less than 0.05). During clomipramine treatment significant decreases were seen on all the six VAS: sadness, bodily discomfort, inner tension, concentration difficulties, memory disturbances and pain. Bodily discomfort and pain were significantly reduced during maprotiline treatment. The effects produced by clomipramine were also significantly greater than the effects caused by

maprotiline as concerns psychic anxiety and inhibition (VAS). The overall reduction in VAS was significantly greater with clomipramine when compared to maprotiline. The most important side effects were dry mouth (both drugs) and sweating (clomipramine). However, in the clomipramine group, 8 patients were excluded due to side effects as compared to 1 patient in the maprotiline group. Thus, the results indicate that antidepressants reduce not only pain but are also of clinical value in the treatment of patients with idiopathic pain syndromes. Drugs with pronounced effects on the serotonin reuptake are to be preferred.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human; Male
Adult
Aged
*Anthracenes: TU, therapeutic use
Clinical Trials
Clomipramine: AE, adverse effects
*Clomipramine: TU, therapeutic use
*Depressive Disorder: DT, drug therapy
Depressive Disorder: PX, psychology
Double-Blind Method
Maprotiline: AE, adverse effects
*Maprotiline: TU, therapeutic use
Middle Aged
***Pain: DT, drug therapy**
Pain: PX, psychology
Pain Measurement
Psychological Tests
Random Allocation

CAS REGISTRY NO.: 10262-69-8 (Maprotiline); 303-49-1 (Clomipramine)

CHEMICAL NAME: 0 (Anthracenes)

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